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CONTENTS OF THIS ISSUE

Camphor from Camphor Basil (*Ocimum kilimandscharicum* Guerke) 153
M. S. Lowman and J. W. Kelly

Incompatibilities in Prescriptions. VI. Hydrolysis of Zinc Salts 163
William J. Husa and Jack K. Dale

Effect of Time and Temperature in the Preparation of Certain Fats and Waxes for Melting-Point Determinations 165
D. M. Copley

Notes on Mexican Drugs, Plants, and Foods. III. Ahuauhtli, the Mexican Caviar . . 170
Marcel Bachstez and Allagracia Aragon

The Subacute Toxicity and Irritation of Polyethylene Glycols of Approximate Molecular Weights of 200, 300, and 400 172
Henry F. Smyth, Jr., Charles P. Carpenter, and C. Boyd Shaffer

Cascara Sagrada Berries, and Adulterant of Buckthorn Berries, N. F. VII 174
Clare Olin Ewing and Albin Stitt

Book Reviews 175

Abstracts 153–176

Advertising—Cover pages, 2, 3, 4, and pp. I to VIII

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Camphor from Camphor Basil (*Ocimum kilimandscharicum* Guerke)*

By M. S. Lowman and J. W. Kelly

INTRODUCTION

Camphor occurs in nature in the essential oils of many plants but all commercial supplies of natural camphor come from the camphor tree, *Cinnamomum camphora* (L.) T. Nees et Ebermaier (*Laurus camphora* L.). Japan has long been the sole supply of this important product, obtained by distillation of the wood and leaves of this tree. The insecurity of complete dependence on a single foreign source was recognized many years ago before the production of synthetic camphor became a commercial possibility. About 1905 the Bureau of Plant Industry began a study of the possibilities of growing the camphor tree in the southern states where trees previously introduced as ornamental shade trees had been found to grow luxuriantly. The results of this investigation led to commercial plantings by two concerns in this country who were interested in a domestic source of supply. About fifteen years later when these plantings had about reached the stage of production the project was abandoned because of the high costs involved and the competition from synthetic camphor which was beginning to replace the natural product. At present our principal commercial supply is synthetic camphor manufactured from pinene obtained from the oil of American turpentine.

The fact that camphor occurs as such in nature in varying amounts in many plants has not been lost sight of in the search for other practical sources of this important product. It is obvious that a herbaceous plant that gives a high yield of "natural" camphor and that can be grown in one season as a farm crop would have certain advantages over the camphor tree which requires several years to come into production or even synthetic camphor which is also dependent on plant products requiring a long time for growth. For this reason an *Ocimum* species, the volatile oil of which has been found to contain a high percentage of camphor, has attracted much attention. Considerable experimental work has been done on the culture of this plant in eastern Africa, Russia, and to a less extent in the United States. The name *Ocimum canum* (L.) Sims has long been erroneously associated with the camphor-yielding basil, and the various oils reported to have been distilled from this species by different investigators show a wide variation in chemical composition as indicated in Table I. More recently, however, Russian botanists have found that plants being grown in Russia for the production of camphor which have been incorrectly called *O. canum* more nearly resemble *O. menthaefolium* Hochst., but a definite identification was not made.

* Received Aug. 16, 1944, from the Bureau of Plant Industry, Soils and Agricultural Engineering, Agricultural Research Administration, U. S. Department of Agriculture, Beltsville, Md.

Previous to the Russian findings a basil grown in Africa which yielded considerable camphor was described as *O. kilimandscharicum* Guerke. The plant under investigation was identical with the original description of *O. kilimandscharicum*.

It is interesting to note that the several species and varieties of *Ocimum* produce oils possessing a variety of odors and flavors, some of which are used as flavoring and scenting agents. The oil of the common sweet basil (*O. basilicum* L.) is used in the flavoring and perfuming industry because of its pleasant spicy odor and taste. Oils produced from other species resemble in odor and flavor the oils of cinnamon, cloves, lemon, and thyme because of certain dominating chemical constituents common to both.

REVIEW OF THE LITERATURE

According to reports by various investigators, the chemical composition of oils supposedly distilled from *Ocimum canum* varies greatly. This wide variation in chemical constituents may be due to the fact that the investigators were working with different species assumed to be the same rather than to the fact that they were grown under different conditions. Errors in botanical identifications of the plants distilled are almost certain to have been made in view of the confusion in the taxonomy of this genus.

Charabot (1), in 1903, described an oil said to have been distilled from *O. canum*, which contained a large proportion of *d*-camphor. Again in 1927 (2) he reported that a volatile oil distilled from plants originating in British East Africa deposited 35% *d*-camphor on cooling and that the oil portion still contained considerable camphor. The plant was identified as *O. canum* by G. Blanque and J. Maheu, who provided a detailed description with drawings. Later Blanque and Maheu (3) gave a more complete description of the same plant from which Charabot distilled the oil containing camphor. Its geographical distribution was outlined and the botanical relationship to other species discussed.

In 1908 Schimmel and Co. (4) reported on an oil from *Basilicum canum* (*Ocimum canum*) which was found to contain considerable *d*-camphor with chemical and physical constants agreeing with those of commercial natural camphor. However, in 1913 Roure-Bertrand Fils (5) reported that an oil distilled from a plant from East Africa, identified by E. G. Camus as *O. canum*, was heavier than water and that on cooling it deposited a mass of large needle-like crystals, which on recrystallizing from 60% alcohol were identified as methyl cinnamate. The fresh herb contained 0.65% oil, 87% of which was methyl cinnamate. A. Chiris (6), in 1924, reports on three samples of oils. Two of them were supposed to have been distilled from *O. canum*, one of which came from the Comoro Islands and the other from Bambari (Central Africa). The first contained 54.19% and the second 78.44% of methyl cinnamate. The third sample of oil obtained from Anjouan in the Comoro Islands, distilled from an unidentified species of the Labiatae unlike *O. canum*, contained approximately 60% of *d*-camphor.

In the same year Glichitch (7) published a complete chemical analysis of one of the oils examined by A. Chiris. The results indicate the following approximate composition: Eucalyptol 1%, free *l*-linalool 25%, estragol 2%, geraniol 0.5%, other alcohols (possibly terpineol) 1%, methyl cinnamate and methyl allo-cinnamate 55%, esters of aliphatic acids in the C_8 to C_8 groups 0.5%, *l*-sesquiterpene 10%, *d*-sesquiterpene 4%, and loss 1%.

In 1925 (8) A. Chiris reported on three additional samples of *O. canum* oils. Two from the Comoro Islands were found to contain 54 to 56% and 78%, respectively, of methyl cinnamate; the others from Bambari (Congo) distilled from young plants contained 29.26% of methyl cinnamate and 25% to 30% of linalool.

Glichitch and Naves (9), in 1933, reported that oils of *O. canum* produced in Mayotte, Kenya, Anjouan (Comoro Islands) and at Antibes (Alpea-Maritimes, France) contained *d*-camphor but no methyl cinnamate, while oils reported to have been distilled from the same species in the Comoro Islands, Madagascar, and Ubangi-Chari all contained considerable methyl cinnamate but no camphor. The source of production also affected the thymol and eugenol content of oils from *O. gratissimum*.

In an anonymous report in *The Bulletin of Imperial Institute* (10), in 1934, the following characteristics for an oil distilled from *O. americanum* Mill. (*O. canum*) are given: sp. gr. at 15.5° C. 0.9181; angle of rotation at 20° C. −3.63°; index of refraction at 20° C. 1.4878; acid value 12.4; aldehydes and ketones (by bisulfite) 71% by volume; aldehyde as citral (by hydroxylamine) 62.3% by wt.; acids and phenols (by absorption with KOH) 8%, and solubility in 70% alcohol 1 in 2.2 vol. with opalescence.

D. P. Snegirev (11), in 1936, reporting on the composition of the oils of *O. canum* hybrids grown experimentally in U. S. S. R., states that camphor was the principal constituent. Thomssen (12) in 1938 comments on a report of the experimental culture in East Africa of *O. canum* which was at first called *O. americanum*. A forty-acre planting had been made and it was found that a first crop could be cut for distillation six months after planting the seed and every three months thereafter. A yield of 0.5% to 0.8% oil containing 65% to 80% camphor was obtained from the fresh herb, or about 400 pounds of camphor-oil mixture per acre. The oil, after removal of the camphor, was said to resemble oil of eucalyptus. Experiments conducted in Florida in 1937, by the same investigator, proved that this plant will yield camphor when grown in this country. Again in 1942, Thomssen (13) further reports on experiments conducted in Minnesota, Florida, southwestern Michigan, and in Alabama where good yields of oils with high camphor content were obtained. The purified camphor was found to meet the U. S. P. requirements for natural camphor.

Knishevetskaya (14), in 1939 and 1940, reported that the oils distilled from 8 hybrids obtained by the hybridization of F_1 *Ocimum* sp. No. 49 x *Ocimum canum* contained borneol, which was not present in the oils distilled from either of the parents; 17.7% of methyl chavicol which was present to the extent of 65% in the oil of the F_1 *Ocimum* sp. No. 49 and 18.2% of camphor present in the oil from the parent *O. canum* to the extent of 65% to 70%.

Reporting on new Indian essential oils, S. Dutt (15), in 1940, describes an oil known as "mamri oil" distilled from the leaves and tender stems of *O. canum*, as containing 60.0% citral and 10.9% of linalool in addition to other constituents named but no camphor or methyl cinnamate was present.

An anonymous report in the *Bulletin of the Imperial Institute* (16) in 1941 described an oil obtained in the Egyptian Sudan by steam distillation of the dried leaves of *O. kilimandscharicum*. A yield of 5% of oil was obtained which contained about 77% of *d*-camphor. The residual oil resembled "light" camphor oil or spike lavender oil.

In a report on the biochemistry of camphor basil Tsarev (17), in 1942, states that camphor occurs in commercial quantities in three different kinds of plants grown in the Soviet Union, namely, the camphor laurel (*Cinnamomum camphora*), astrachan wormwood (*Artemisia maritima* var. *astrachanica*), and the camphor basil. He states that the camphor-producing basil has from the beginning been wrongly designated *O. canum*. Recently V. N. Voroshilov (Vilar) and Prof. B. A. Fedchenko (Bin) suggested that this plant in their opinion more nearly corresponded to *O. menthaefolium* Hochst. The lack of more complete herbarium material prevented a more definite determination. A study of the oil distilled from this plant showed the principal constituent to be *d*-camphor about 65% together with twelve other compounds named. Experiments concerning the accumulation of oil in different parts of the plant at various stages of growth were described. The influence of size and location of leaves on the plant and the effect of light and drying on the oil and camphor content were discussed.

THE BOTANICAL DESCRIPTION OF THE CAMPHOR BASIL PLANT[1]

This species of basil is native to Kenya, East Africa. After it was discovered that the plant contained camphor, it was distributed to various other countries and grown under the name *Ocimum canum* Sims in error. *O. canum* is an annual plant, the seed of which was sent to England from China. Incorrect identification of the camphor basil has caused considerable confusion in the literature. It appears that at least two other plants have been called *O. canum*, causing even more confusion. In a report in the *Bull. Imp. Inst.*, previously referred to (16), the following statement occurs: "*Ocimum kilimandscharicum* does not appear to occur in the wild state in the Sudan and material from which the oil has been obtained originated from plants sent from Kenya. These appear to have been sent originally as *O. canum*, but the plant in question was definitely identified later at Kew as *O. kilimandscharicum*."

Although the camphor basil, *Ocimum kilimandscharicum* Guerke is described as an undershrub in its native habitat, it has been grown at Arlington Farm, Va., and Beltsville, Md., as an annual. The plant grows well from seed or cuttings and apparently can be handled as an herbaceous perennial in places where the ground does not freeze. The plant as grown at Beltsville, Md., has the following characteristics:

General Habit of Growth.—Much branched from just above the base, giving the appearance of a small bush with many leaves and with flower stalks terminating the branches. The numerous white hairs (1 to 2 mm. long) on the stems and leaves give the plant a gray-green appearance when light conditions are favorable.

Stems.—Forty-five to 75 cm. long, sub-quadrangular to nearly terete, brown, more or less hairy with spreading white hairs which are sometimes mixed with shorter hairs curled downward and inward. The older stems tend to lose their hairs near their bases and the bark becomes shredded and conspicuous when the dry stems are broken.

Leaves.—(Only the larger leaves near the middle of the stems of typical plants at flowering time are described here.) Ovate to ovate-lanceolate, 3 to 7 cm. long, including petioles which are 4 to 12 mm. long, 1 to $2^1/_2$ cm. wide, more or less appressed hairy on both sides, petioles slender and long hairy at least when young, acute at the summit and narrowed to a cuneate base. The upper two-thirds of the blade is more or less crenate-serrate to nearly entire in some of the narrow-leaved forms. Each square millimeter of leaf surface on both sides contains about 14 amber-colored oil glands. The leaves of winter-grown greenhouse plants differ in having petioles up to $3^1/_2$ cm. long, are mostly obtuse at the summit and are nearly glabrous except for a few scattered hairs on the principal veins beneath. Margins of the blade entire, crenate or crenate-serrate.

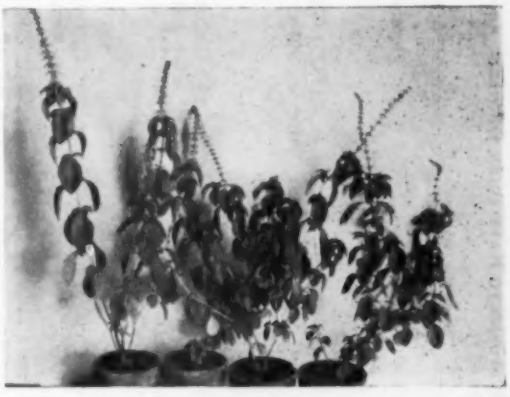

Fig. 1.—Camphor Basil (*O. kilimandscharicum* Guerke) Grown in the Greenhouse from Stem Cuttings.

Flowers.—Borne in 15 to 30 cm. long spike-like pubescent racemes at the ends of the branches (Figs. 1 and 2). The flower whorls are mostly about 1 to 2 cm. apart and normally bear six flowers each but sometimes only 2 or 4 flowers are found in each whorl. The flowering stems stand above the main mass of foliage during mature stages. Individual flowers are borne on short, nearly erect hairy pedicels. In fruit these pedicels become reflexed at the summit so that the calyx hangs from its point of attachment. Each flower whorl bears two small leaf-like bracts at their bases. These persistent bracts are 4 to 6 mm. long, orbicular to ovate-lanceolate, acuminate at the tip and abruptly narrowed to a petiole-like base. The campanulate calyx is 3 to 4 mm. long at anthesis, upper lobe orbicular and apiculate, lower lobe 4-toothed, the two lateral teeth ovate and abruptly short acuminate, the lower teeth close together, lanceolate-subulate and longer. The creamy-white corolla is two to three times the length of the calyx, stamens and style long exserted, style equally bifid at the apex. The upper filaments bear a hairy tooth near the base. The seeds are black, about $1^1/_4$ mm. long and minutely roughened.

EXPERIMENTAL

Cultural studies were begun in the spring of 1937 with a small lot of seed furnished by a dealer in essential oils in this country, who was interested in the possibilities of this crop. This seed probably originated in East Africa. Experiments concerning the cultural requirements and the effects of various factors on the yield and quality of the essential oil were made in field plots and laboratory studies at Beltsville, Md., and Arlington Farm, Va.

[1] Credit is due O. M. Freeman, Bureau of Plant Industry, Soils and Agricultural Engineering, for identification of the plant and the botanical description.

TABLE I.—DATA SHOWING DIFFERENCES IN CHEMICAL AND PHYSICAL QUALITIES OF OILS SUPPOSED TO HAVE BEEN DISTILLED FROM *Ocimum canum* AS REPORTED BY VARIOUS INVESTIGATORS

Investigator	Date	Source of Oil	Yield of Oil and Chemical Constituents	Physical and Chemical Constants
E. Charabot	1903	British East Africa	Large proportion of *d*-camphor. 35% camphor on cooling	
	1927	British East Africa		
Roure-Bertrand Fils	1913	Africa	0.65% in fresh herb, 87% methyl cinnamate	Sp. gr. 32° C. 1.0330; angle rot. 30° C. −2° 30′; acid value 0; ester value 301.4; soluble in 2.25 vol. 75% alc.
Schimmel & Co.	1908	Mayotte Island	Large proportion of *d*-camphor, practically no esters	
A. Chiris	1924	Comoro Islands	Eucalyptol 1%; free *l*-linalool 25%; estragol 2%; geranol 0.5%; other alcs. 1%; methyl and methyl allocinnamate 55%; esters of aliphatic acids in C_4 to C_8 group 0.5%; *l*-sesquiterpene 10%; *d*-sesquiterpene 4%; and loss 1%[a]	Sp. gr. 15° C. 0.987; angle rot. −5° 4′; acid value 0.42; ester value 186.2, after formulation 280.0; index ref. 20° C. 1.52492
	1924	Bambari (Congo)	78.44% methyl cinnamate; terpene constituent *l*-rotatory	Sp. gr. 20° C. 1.0412; angle rot. 1° 30′; acid value 0.68; ester value 269.5; index ref. 20° C. 1.54852
	1924	Anjouan[b] (Comoro Islands)	62% *d*-camphor, alc. (as borneol) free 4.73%, alc. (as borneol) comb. 1.84%, residual oil 5% eugenol	Sp. gr. 28° C. 0.9352; angle rot. 28° C. 42° 38′; ester value 6.7, after acetal. 26.52; residual oil angle rot. 26° C. 32° 30′
	1925	Comoro Islands	78% methyl cinnamate	
		Bambari (Congo)	54 to 56% methyl cinnamate	
		Bambari (Congo)	29.26% methyl cinnamate and 25 to 30% linalool	
Bull. Imp. Inst.	1934		Aldehydes and ketones (by disulfite) 71% by vol. Aldehyde as citral (by hydroxylamine) 62.3% by weight acids and phenols (by absorption with KOH) 8%	Sp. gr. 15.5° C. 0.9181; angle rot. 20° C. −3.63°; index ref. 20° C. 1.4878; acid value 12.4; sol. in 70% alc. 1 in 2.2 vol. with opalescence
E. G. Thomssen	1938	East Africa	0.5 to 0.8% in fresh herb, 80% *d*-camphor	
	1938	Florida	0.5% in fresh herb, 47.2% *d*-camphor	Oil freed from camphor sp. gr. 25° C. 0.9251; angle rot. 20° C. −0.38°; index ref. 20° C. 1.4750; ester value 11.4
	1942	Minnesota	0.5% in fresh herb, 50% *d*-camphor	
S. Dutt	1940	India	0.6 to 0.7% in fresh herb; linalool 10.9%; esters 4.8%; geraniol and citronellol 7.3%; methylheptone 2.4%; citral 60%; citronellal 7.3%; unidentified const. 4.8% and residue 2.4%	

[a] Analysis by L. S. Glichitch (7). [b] Species undetermined but differed from *O. canum*.

Propagation and Culture.—In the first experimental planting made by the Division of Drug and Related Plants at Arlington Farm, Rosslyn, Va., on May 11, 1937, the seed was drilled directly in the field in rows 3 feet apart and at the rate of 20 to 30 seed to the foot. At this rate 2 to 3 pounds of seed will plant an acre. A good stand of plants came up in about ten days. The soil at Arlington Farm is a clay loam, flat and poorly drained.

Plants grown in the greenhouse from seed sown early in April were set in the field in May. The plants spaced a foot apart in rows 3 feet apart produced solid rows 3 feet high by midseason. They began blooming about two weeks earlier than the field-sown seedlings. Plantings were also made in 1938 and 1939 (Fig. 3) with both greenhouse-grown plants and direct field sowing. On land that is very weedy direct field seeding requires considerable hand work to control the weeds until the small seedlings are large enough to be cultivated.

In the spring of 1942 and 1943 (Fig. 4) experimental plantings were made at Beltsville, Md., on sandy loam soil with greenhouse-grown plants and by direct field seeding in rows. The greenhouse-grown plants began blooming about two weeks earlier than those obtained from field-sown seed.

Yield of Herb.—Table II gives data comparing the yields of herb and oil obtained at different stages of maturity by the two methods of propagation. More herb was obtained in the early part of the season from the field-set plants but the total yield for the season was about the same for both types of planting. The yields of herb tended to decline after the full blooming period was reached about the latter part of August, except in the case of the September 14 harvest of the field-set plants. This appeared to be due to the loss of the lower leaves as the plants mature, which apparently is not compensated for by the gain in new growth at the top. The figures are based on the weight of herb cut from only a short section of a row in each case and therefore should be considered as only an indication of what may be expected on a larger area.

Two harvests cut in one season from a 68-foot row of greenhouse-grown plants gave a combined yield approximately the same as the yield obtained from one harvest cut at the full flowering stage. The first harvest from the 68-foot row was cut on July 20 when only a few flowers were open and the second growth was cut on September 23 when the plants were about 30 inches high and almost in full bloom. The first cutting yielded 90.2 pounds and the second 112.5 pounds of fresh herb, or a total of 202.7 pounds for the season, equivalent to 43,282 pounds per acre. This is only slightly in excess of the maximum yield shown in Table II from one harvest cut on August 23 at the full bloom stage.

Distillation and Yields of Oil and Camphor.—Considerable difficulty was experienced in the distillation and collection of the oil and camphor mixture. Attempts were made to distill the fresh herb with steam, using a tubular type condenser frequently used in the distillation of essential oils. Camphor rapidly deposited on the cold walls of the tubes, completely clogging them, even when the temperature of the condensate was kept near the boiling point of water. The use of this type of condenser was not satisfactory. Another type which was used in the distillation of leaves from the camphor tree in Florida was tried. This condenser consisted of a cylindrical metal receiving vessel about 12 inches in diameter and 18 inches high, fitted with a cooling coil and connected at the bottom with the head of the retort. A small cold-water jet placed at the bottom of the vessel so that a spray of cold water met the hot distillate as it emerged from the pipe leading from the retort, served to help condense the vapors and also to regulate the flow of distillate containing the camphor-oil mixture, from the overflow outlet at the top of the receiver. The temperature of the distillate was regulated both by means of the cooling coil and the cold-water jet. The apparatus successfully condensed the oil and camphor-laden vapor but considerable of the camphor formed in a finely divided suspension and the oil emulsified with the water to such an extent that the apparatus was discarded as unsatisfactory.

A small laboratory distilling outfit consisting of a Remington retort and head fitted with a 24-inch Liebig condenser was assembled for trial tests. The receiver consisted of a 1 x 10-inch test tube with a

Fig. 2.—Flower Spike of Camphor Basil (*O. kilimandscharicum* Guerke) about Natural Size.

1/4-inch hole in the bottom, standing in a suction flask, the side connection of which served as an overflow. The length of the tube was sufficient to extend above the top of the suction flask. The retort held from 15 to 16 pounds of fresh or 6 to 8 pounds of dried herb. Successive trial distillations proved that the oil and camphor could be completely removed from the herb and recovered as a semisolid mass by means of this apparatus. The herb was firmly packed into the retort and dry steam admitted at such a rate as to keep the temperature of the distillate emerging from the condenser at about 90° C. At this temperature the camphor-oil mixture was completely condensed and maintained a consistency that allowed it to flow from the smooth glass wall of the condenser to the receiving tube without serious clogging. The camphor-oil mixture remained in a semisolid state in the receiving tube during the distillation, and on cooling the contents could be removed from the tube in a solid plug for weighing.

[a] Analysis by L. S. Glichitch (7). [b] Species undetermined but differed from *O. canum*.

TABLE II.—YIELDS OF HERB, OIL AND CAMPHOR AT DIFFERENT STAGES OF MATURITY OF PLANTS GROWN FROM SEED SOWN BOTH DIRECTLY IN THE FIELD AND IN THE GREENHOUSE AND TRANSPLANTED TO THE FIELD AT BELTSVILLE, MD., IN 1943

Date of Harvest	Method of Propagation[a]	No. Ft. of Row Cut	Pounds Fresh Herb		Oil and Camphor				Camphor			
					Per Cent in Fresh Herb		Pounds per Acre		Per Cent in Oil from		Pounds per Acre from	
			Distilled	Per Acre Calculated	Distilled Fresh	Distilled Dry[b]	Distilled Fresh	Distilled Dry	Fresh Herb	Dry Herb	Fresh Herb	Dry Herb
July 27	A	30	36.56	17,695	0.45	0.58	79.63	102.63	63.0	70.1	50.17	71.95
	B	20	33.50	24,321	0.66	0.75	160.52	182.41	58.3	60.6	93.58	110.54
Aug. 5	A	20	32.00	23,232	0.58	0.68	134.75	157.98	68.0	68.2	91.63	109.74
	B	16	26.87	24,384	0.65	0.72	158.50	175.56	64.6	69.9	102.39	122.72
Aug. 23	A	16	43.25	39,249	0 70	0.81	274.74	317.92	66.0	70.2	181.33	223.34
	B	16	45.75	41,518	0.81	0.92	336.30	381.97	67.6	69.9	227.39	267.00
Sept. 6	A	70	152.25	31,581	0.48[c]	0.65	151.59	205.28	60.3	60.5	91.41	124.20
	B	84	176.00[d]	30,423	0.55	..	167.33	....	61.3	..	102.57	....
Sept. 14	A	20	42.00	30,492	0.43	..	131.12	....	50.8	..	66.61	....
	B	28	85.00	44,078	0.50	..	230.39	....	52.3	..	115.26	....

[a] A = seed sown directly in the field on May 13; B = plants grown from seed in the greenhouse and transplanted to the field on May 11.
[b] Half of each lot was air dried before distillation.
[c] Fresh herb incompletely distilled.
[d] 76 pounds distilled.

Table II contains the data on the results of distillations of both fresh and dried herb from field-set plants and plants grown from field-sown seed at various stages of maturity. The herb from plants set had a consistently higher oil content than the herb from field-sown seed. This was due apparently to the higher proportion of leaves in the field-set plants since they were not as closely spaced in the row and therefore had more room for developing. There was a distinct advantage in drying the herb before distillation as may be observed from the yields of oil and camphor obtained. The oil could be more quickly and thoroughly distilled from the dried herb because the herb in the fresh state contains about 80% of moisture which adds to the total mass to be heated to the distillation point. There evidently was no appreciable loss of oil or camphor on drying but, on the contrary, the dry herb in each case gave better yields of oil with a higher camphor content because it could be more completely exhausted. Incomplete removal of the oil from the herb resulted in oils low in camphor since the last fractions of the oil that distills over contained the highest proportion of camphor. The camphor content of the oils from the various distillations made was not uniform but it did not appear to be related to the stage of maturity of the plants. A 32-pound lot of herb cut on September 23, during the seed-ripening stage, was dried and distilled and yielded 0.70% of oil with 57.2% of camphor. After a killing frost the middle of October, about 5 pounds of frozen flowering tops which had been partially dehydrated by freezing were cut and distilled. A yield of 2.10% oil containing 63.2% of camphor was obtained. At the same time 17.5 pounds of fresh frozen herb, less some large stems, were dried and distilled. The yield of oil and camphor mixture was 0.84% on the fresh basis, 61.5% of which was camphor. About the middle of November after the plants were completely defoliated a half pound of the dead and partially decayed leaves, raked from the ground and distilled, yielded considerable oil containing 79% of camphor. The loss of the more volatile fractions of the oil resulted in a concentration of camphor in the oil remaining in the dead leaves. Based on these results the maximum yield of camphor per acre would be obtained by distilling the dried herb cut at the stage of maturity which gives the greatest weight of herb with a minimum of stems. The large stems are entirely devoid of oil and the small succulent stems contain only small quantities so the most branching leafy type plants give the highest yield of oil.

Distillation of Individual Plants.—In order to learn something of the relation of oil content to individual plant variations, a number of plants representing different types were distilled individually at various stages of maturity. The method used for these determinations was a modification of the distillation method using the oil separatory trap as described in the Official and Tentative Methods of Analysis of the Association of Official Agricultural Chemists, 1940, page 470. A 10-liter, wide-mouth, round-bottom flask with a glass tube extending through the stopper to the bottom for admitting the steam was used for the retort. This apparatus designed for volatile oil determinations on small quantities of material provided for the continuous automatic return of the distillate water to the retort after the separation of the oil. Thus at the end of the distillation, which required about one hour, all of the oil and camphor contained in the herb had collected in the receiver and after cooling was removed in a solid plug and weighed.

The herb from each plant was weighed fresh, the leaves and stems of over 5 mm. in diameter separated to determine the proportion of leaves and stems

stems. The leaves with small stems attached were coarsely chopped immediately before distillation to facilitate packing in the round-bottom retort flask. Steam was admitted through the glass tube to the bottom of the retort. A small amount of water added to the flask previously was kept boiling by means of a Bunsen burner to prevent excessive condensation of the steam in the retort. The temperature of the distillate in the receiving tube was kept at about 90° C. in order to prevent solidification of the camphor oil mixture and clogging of the apparatus. Test distillations of large, medium and small stems showed that only traces of oil could be separated from the smallest stems while the larger ones were entirely devoid of oil.

separated and the leaves with small stems attached were crushed and distilled as described above. The results given in Table IV show that there is some variation in oil content between individual plants when calculated on either the fresh or air-dried basis or on the dried herb with all stems above 3 mm. in diameter removed. The average percentage of oil calculated on the whole fresh plant basis was about the same as that obtained by distilling the fresh plants. This does not agree with the results in Table II where it was shown that better yields of oil were obtained by distillling the dried herb. This difference in results was probably due to the fact that the distillation of individual plants by means of the apparatus described completely removed the

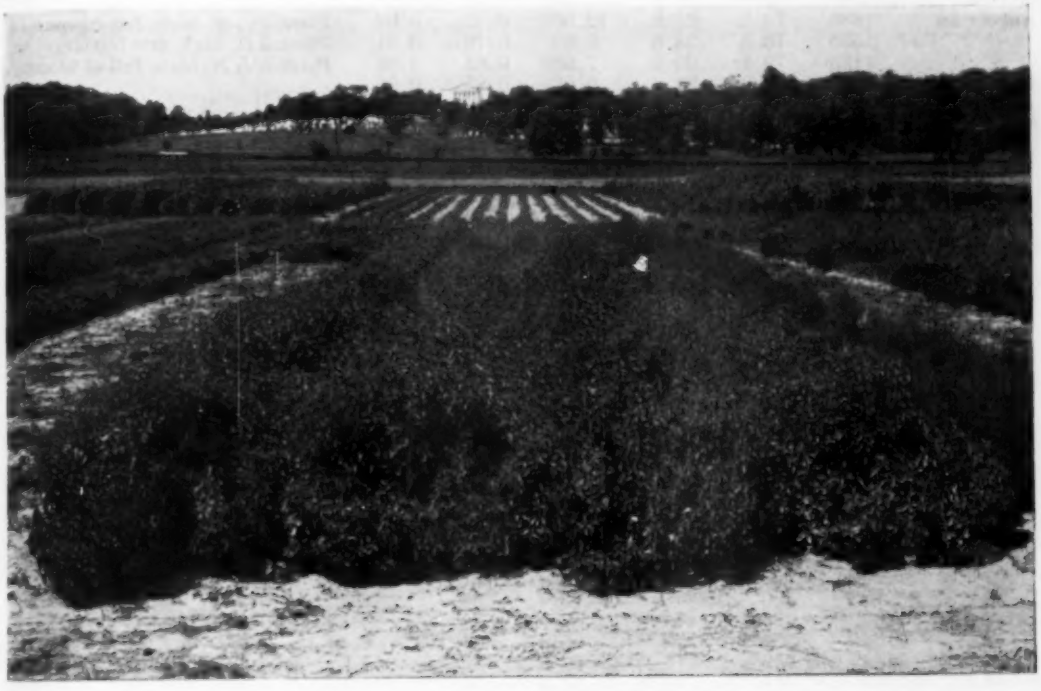

Fig. 3.—Camphor Basil (*O. kilimandscharicum* Guerke) from Seed Sown Directly in the Field in Rows One Meter Apart at Arlington Farm, Va. Photographed in the Early Flowering Stage on August 22, about Three Months from Seeding.

Examination of the data in Table III indicates some variation in the oil content of individual plants, only part of which is accounted for by the variation in proportion of stems and leaves. There is a definite increase in size of plants, percentage of oil in the leaves and weight of oil per plant as the plants mature. The average percentage yield of oil in the leaves increased from 0.74% for the July 29 harvest to 0.93% for the September 1 harvest. The maximum blooming stage occurred late in August or early in September. Flowering began about the middle of July and continued until frost. The lower leaves began to fall soon after the maximum flowering period was reached. A light crop of seed was harvested from plants left standing until killed by frost.

On September 6, ten plants were selected at random, weighed fresh and then dried for ten days on screens in an attic room. The dried herb from each plant was weighed and the loss in weight on drying recorded. The stems over 3 mm. in diameter were

oil from both the fresh and dried herb. Since the complete removal of the oil from the fresh herb required a longer period of distillation than the dried herb, the distillation, using the Remington retort, involved a larger volume of distillate from which it was more difficult to completely recover the oil and camphor mixture.

Separation of the Camphor from the Oil.—The camphor-oil mixture as it came from the still was a colorless semisolid mass of fine granular camphor mixed with the oil. Considerable of the camphor was in solution in the oil. On standing in an electric refrigerator at about 40° C. for twenty-four hours some of the dissolved camphor crystallized out forming a more solid mass. This mass was transferred to a small, basket-type centrifuge lined with filter paper and centrifuged for five minutes. The almost pure snow-white granular camphor was removed from the centrifuge and weighed. Repeated tests of purity made by pressing the camphor in a Carver press at 15,000 pounds per square inch

TABLE III.—THE RELATION OF OIL CONTENT TO INDIVIDUAL PLANT TYPES AT SEVERAL STAGES OF MATURITY

Date of Harvest	Gm. Fresh Herb per Plant	Per Cent		Oil[a]			Description
		Leaves	Stems[b]	Gm. per Plant	Per Cent in Leaves	Per Cent in Whole Plant	
July 29	930	85.5	14.5	5.47	0.69	0.59	Dark green, smooth oval leaf
	790	82.6	17.4	4.56	0.70	0.58	Light green, smooth oval leaf
	705	85.5	14.5	4.96	0.82	0.70	Light green, narrow leaf
	550	87.5	12.5	3.20	0.67	0.58	Large, dark green, oval leaf
	715	92.7	7.3	4.57	0.69	0.64	Small, dark green, oval leaf
	735	84.9	15.1	5.47	0.88	0.74	Large pale green, oval leaf
Average	737	86.3	13.7	4.71	0.74	0.64	
July 31	679	92.3	7.7	6.10	0.97	0.90	Plant short, large leaf
	1005	90.7	9.3	7.38	0.81	0.73	Plant tall, pointed dark green leaf
	1375	84.9	15.1	9.40	0.80	0.68	Plant tall, pointed pale green leaf
Average	1020	88.4	11.6	7.63	0.86	0.77	
August 28	1886	74.2	25.8	12.90	0.92	0.68	Plant 3½ ft. high, few blooms
	1535	76.5	23.5	9.30	0.79	0.61	Plant 3 ft. high, few blooms
	1125	79.1	20.9	7.60	0.85	0.68	Plant 3½ ft. high, full of blooms
Average	1515	76.2	23.8	9.93	0.85	0.66	
August 30	2257	75.8	24.2	16.64	0.97	0.74	Plants all about full bloom, and
	1095	76.0	24.0	8.75	1.05	0.80	differences such as leaf size and
	2287	76.8	23.2	17.30	0.98	0.76	color less evident
	1840	81.8	18.2	12.00	0.80	0.65	
Average	1870	77.6	22.4	13.67	0.95	0.74	
September 1	1868	82.8	17.2	14.74	0.95	0.79	Plants 3½ ft. high, full of bloom
	1010	75.4	24.6	6.20	0.83	0.61	Plants 3 ft. high, few blooms
	1000	80.5	19.5	7.23	0.90	0.72	Plants 3½ ft. high, few blooms
	1475	78.7	21.3	12.30	1.06	0.83	Plants 3 ft. high, full of blooms
Average	1338	79.3	20.7	10.12	0.93	0.74	

[a] Oil-camphor mixture. [b] Over 5 mm. in diameter.

TABLE IV.—THE EFFECT OF DRYING HERB FOR TEN DAYS ON SCREENS IN AN ATTIC ON OIL YIELD FROM TEN INDIVIDUAL PLANTS SELECTED AT RANDOM AT THE LATE FLOWERING STAGE ON SEPTEMBER 6

Plant No.	Gm. Herb per Plant		Per Cent Moisture	Per Cent[a]		Gm. Oil per Plant	Per Cent Oil		
	Fresh	Dry		Leaves	Stems[b]		Fresh Basis, Whole Plant	Dry Basis	
								Leaves	Whole Plant
1	1755	402	77.1	65.2	34.8	11.48	0.65	4.39	2.86
2	1359	304	77.7	72.4	27.6	10.20	0.75	4.64	3.36
3	2158	450	79.1	65.3	34.7	12.73	0.59	4.33	2.83
4	1530	385	74.8	69.4	30.6	13.35	0.87	5.00	3.47
5	1164	304	73.9	65.8	34.2	9.40	0.81	4.54	3.09
6	1446	352	75.7	69.3	30.7	10.02	0.69	4.11	2.85
7	1419	341	76.0	63.9	36.1	10.53	0.74	4.84	3.09
8	1305	317	75.7	60.0	40.0	8.26	0.63	4.35	2.61
9	1419	334	76.5	64.4	35.6	9.70	0.68	4.52	2.91
10	1560	356	77.2	65.7	34.3	10.34	0.66	4.41	2.90
Av.	1511.5	354.5	76.4	66.1	33.9	10.60	0.71	4.51	3.00

[a] Calculations made on the air-dried herb.
[b] Over 3 mm. in diameter.

TABLE V

Fraction, ° C.	Per Cent of Total	Sp. Gr., 30° C.	Index Ref., 30° C.	Angle Rot., 30° C.	Sol. in 80% Alc.	Ester Value	
						Before Acetal.	After Acetal.
140–170	8.8	0.88664	1.4675	+48.8	1 in 8 vol.	9.0	24.3
170–180	12.1	0.89726	1.4681	48.1	1 in 1 vol.	8.3	21.5
180–189	30.5	0.90063	1.4685	47.4	1 in 0.75 vol.	4.7	20.1
189–208	44.3	0.92110	1.4690	44.6	1 in 0.5 vol.	4.2	28.5
Residue	4.3	0.92620	1.5080	40.8	Insol.	8.0	36.8

showed a purity of about 96%. The oil remaining after removing the camphor with the centrifuge was set aside at 40° C. for an additional twenty-four hours and again centrifuged and this operation repeated a third time to complete the removal of the crystallizable camphor at 40° C. The amount of camphor remaining thereafter in the oil was determined by first fractionating the oil at atmospheric pressure. The fraction boiling between 189° and 208° C. which contained the camphor was cooled to

0° C. and the camphor removed by centrifuging or by suction filter. By repeating the freezing and centrifuging three times practically all of the camphor was removed from the fraction. A number of these tests on several oil samples showed that about 20% of camphor still remained in the oil before fractionation. The figures regarding camphor, in Table II, are totals obtained by repeating the cooling and centrifuging process three times at 40° C. and correcting for the 20% of camphor remaining in the oil after this processing.

The camphor as removed from the oil was in the form of snow-white granular crystals which formed white opaque cakes when pressed in a Carver press at 14,000 to 15,000 pounds per square inch. On standing in sealed glass jars the pressed cakes gradually became translucent as the small crystals coalesced to form a solid cake identical in odor and physical appearance to natural camphor. Any contact with metallic substances either in the distilling operation or in the centrifuging process resulted in discoloration of the oil and camphor.

Chemical and Physical Constants.—The oil and camphor mixture as separated from the distillate water was a colorless semisolid mass consisting of granular camphor crystals and a colorless oil. The specific gravity of the mixture taken at 90° C. (clear sol. at 90° C.) and corrected to 30° C. was 0.9359. The angle of rotation in alcohol solution at 30° C. was +40.80° C. The partly decamphorized oil which still contained about 20% camphor in solution had the following constants: sp. gr. at 30° C. 0.9146; angle of rotation at 30° C. +41.3°; index of refraction at 30° C. 1.5709; solubility in 80% alcohol 1 in 1 vol. with clear solution but turbid in more; acid no. 0.6; ester no. 9.36 before and 28.6 after acetylization. The fractions of this oil distilled at atmospheric pressure gave constants as shown in Table V.

The fraction distilling over from 189° to 208° C. contained practically all the remaining camphor in the oil. The constants were taken on this fraction after removal of the camphor portion by freezing. All of the distilled fractions were colorless but the residue was a viscous, reddish colored oil.

The camphor, after purification by repeated crystallizations from alcohol, possessed constants agreeing closely with natural commercial camphor as follows: m. p., 174° to 175° C.; optical rotation at 30° C. taken in alcohol solution, +42° to +44°. The purified camphor possessed the characteristic odor and taste of natural camphor. It crystallized in white granular crystals which formed into a translucent mass when pressed.

Fig. 4.—Camphor Basil (*O. kilimandscharicum* Guerke) at the Beginning of the Flowering Period at Beltsville, Md., from Direct Field-Sown Seed (5 Rows on Right) and Greenhouse-Grown Plants (2 Rows on Left).

DISCUSSION

The results of preliminary experiments on the culture of camphor basil (*Ocimum kilimandscharicum*) indicate that under favorable conditions it has possibilities as a domestic source of natural camphor. The growing season is 120 days or more and it appears that this plant might be grown as an annual crop in some localities or possibly as a perennial in southern sections where the ground does not freeze. Additional cultural tests are necessary to determine what sections of the country are best suited to its culture. The plant can be propagated by seed sown directly in the field, in seed beds and the young seedlings transplanted, or by vegetative cuttings. The crop probably could be handled in the same manner as the experimental planting by cutting at the

blooming stage and distilled somewhat like mint either from the fresh or dried herb. The high percentage of camphor contained in the oil causes clogging of the regular coil or tubular type condensers and some modified type of condenser will have to be devised to collect the semisolid oil and camphor mixture.

Most of the industrial camphor used in the United States is the synthetic product, although in normal times we import annually, principally from Japan, from one to two million pounds of natural camphor. Based on an average of 100 pounds of camphor per acre from camphor basil, 10,000 to 20,000 acres would be required to supply this amount.

The cost of handling the crop in the south as a perennial should not be greater than that of mint in the mint-producing sections of Michigan and Indiana. As an annual the cost no doubt would be somewhat greater. The average yield of peppermint oil in those states is 30 to 40 pounds while camphor basil may be expected to yield from 200 to 300 pounds of camphor-oil mixture per acre. On this basis the cost of producing camphor basil oil would be about one-seventh the cost of peppermint oil. A price of about 40 cents per pound for camphor basil oil would be equivalent in returns per acre to $3.00 per pound for peppermint oil.

SUMMARY

1. Experimental plantings of camphor basil (*Ocimum kilimandscharicum* Guerke) were made at Arlington Farm, Va., and Beltsville, Md., to determine the possibilities of this plant as a domestic source of natural camphor.

2. A review of the literature indicates considerable confusion in naming of species, varieties and correct identity of material in the various countries where the plants are being grown.

3. The species under investigation was identified as *Ocimum kilimandscharicum* Guerke.

4. The plant requires about 90 days from seeding to flowering stage and 120 or more days to mature seed, is perennial but will not survive freezing temperatures.

5. By steam distillation the fresh flowering herb yielded 0.5 to 1 per cent oil including the camphor. Calculated yields from small experimental plots ranged from 100 to more than 300 pounds of camphor-oil mixture per acre. This semisolid mixture contained 50 to 70 per cent of camphor which was easily separated from the oil portion by repeated cooling and centrifuging.

6. The physical and chemical constants of the purified camphor agreed closely with commercial natural camphor.

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Incompatibilities in Prescriptions. VI. Hydrolysis of Zinc Salts*

By William J. Husa† and Jack K. Dale

Many of the incompatibilities of zinc salts are caused by the slight acidity of aqueous solutions due to partial hydrolysis (1). Published data on the *p*H of solutions of zinc salts are incomplete and contradictory. The purpose of the present study was to clear up some of the discrepancies and to obtain more complete data. Experiments were also conducted to determine the effects of heating, storage and recrystallization on the *p*H of solutions of zinc salts.

In 1907, Denham (2) made the first extensive application of the hydrogen electrode to the study of hydrolysis. Difficulties arose on account of the reducing action of hydrogen on the ions of the less active metals and on some anions such as chlorates and nitrates. Solutions of zinc chloride and zinc sulfate apparently did not reach equilibrium in sixteen days, as the *p*H varied irregularly from day to day. The explanation given was that hydrolysis of these salts led to heterogeneous systems, in which the hydroxide or basic salt of zinc was present in colloidal form. About twenty years later, Denham and Marris (3) found that the *p*H of *M*/100 zinc sulfate solutions as shown by the hydrogen electrode was 5.09. However, they concluded that the results with the hydrogen electrode were in error due to reduction of divalent zinc ions to monovalent ions.

There is a lack of agreement in the results obtained with the quinhydrone electrode by various workers. For *M*/100 zinc sulfate solution, Quintin (4) reported a *p*H of 5.52 as compared with a later value of 6.57 obtained by Dupont (5).

Kolthoff and Kameda (6) found the *p*H of *M*/10 zinc sulfate solution to be 5.67 by the hydrogen electrode and 5.66 by the colorimetric method using methyl red. Both methods gave a *p*H of 6.00 for *M*/100 zinc sulfate solution. These authors concluded that for concentrations above *M*/10, no method could give reliable results, due to free acid error with quinhydrone and salt error in the hydrogen electrode and colorimetric methods.

The glass electrode was applied to the study of hydrolysis of solutions of zinc sulfate by Hagisawa (7) and Brown and Cranston (8). For *M*/10 zinc sulfate solution exposed to the air, Brown and Cranston reported a *p*H of 5.67; this result agrees with the value obtained by Kolthoff and Kameda (6).

It is apparent that salts other than the sulfate have been largely neglected in past studies on the *p*H of solutions of zinc salts.

EXPERIMENTAL

Materials Used.—Zinc salts of all available grades from the official grade to reagent grade were purchased from representative manufacturers subsequently designed as A, B and C. The water used in making solutions was freshly prepared redistilled water meeting the standards of Redistilled Water, N. F. VII.

Determination of *p*H.—Determinations of *p*H were made with the glass electrode. The apparatus employed was the Beckman *p*H meter, laboratory model G, using 2½-inch internal electrodes. In each case the first *p*H readings were made after the freshly prepared solutions had been allowed to stand for one hour.

Variation in *p*H in Products of Different Manufacturers.—The *p*H of a salt purchased on the market should not be regarded as a constant since there may be a variation depending on the control methods of the manufacturer. Thus the *p*H of a salt may vary according to the *p*H of the solution from which it was crystallized. In our study of the products of three manufacturers, the salts made by one manufacturer usually gave slightly higher *p*H values than the others, as shown in Table I.

TABLE I.—VARIATION IN *p*H VALUES OF ZINC SALTS OF DIFFERENT MANUFACTURERS

Solution	Manufacturer A	B	C
M/10 zinc chloride, U. S. P.	6.16	6.16	6.20
M/10 zinc nitrate, reagent	5.52	5.38	5.97
M/10 zinc sulfate, U. S. P.	4.47	...	5.72
M/10 zinc acetate, U. S. P.	6.51	6.51	6.51

Variation in *p*H in Different Grades of Salt.—The results in Table II indicate a tendency for the *p*H of the U. S. P. grades of zinc salts to be slightly higher than for salts of reagent grade.

Average *p*H Values of Zinc Salts.—The average *p*H values found for three different concentrations of each zinc salt when freshly prepared, as well as after 2 and 4 days' storage, are presented in Table III. Each *p*H value is the average of numerous determinations on several different samples of each salt.

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† Head, Department of Pharmacy, University of Florida.

Effect of Recrystallization on *p*H.—Zinc sulfate of reagent grade was recrystallized three times from a mixture of redistilled water and alcohol. The crystals were then carefully washed with redistilled water and dried in a desiccator over anhydrous zinc sulfate. The *p*H of an *M*/10 solution of the original crystals was 5.08 and for an *M*/10 solution of the thrice-recrystallized salt the *p*H was also 5.08, thus indicating that recrystallization had no effect on the *p*H.

Effect of Heating on *p*H.—An *M*/10 solution of zinc sulfate of reagent grade was heated at 100° C. for one hour. During the heating period the *p*H was raised from 5.08 to 5.18. A similar solution of *p*H 5.02 was found to have a *p*H of 4.83 after heating for ten hours at 100° C. Each experiment was conducted twice. From these results it would seem that heating for short periods drives off some carbon dioxide, thus slightly raising the *p*H. Heating for longer periods lowers the *p*H by increasing the hydrolysis of the zinc salt.

TABLE II.—VALUES OF *p*H FOR *M*/10 SOLUTIONS OF ZINC SALTS OF DIFFERENT GRADES

Salt	U. S. P. Grade	Reagent Grade
Zinc chloride	6.17	6.12
Zinc sulfate	5.10	4.96
Zinc acetate	6.51	6.52

DISCUSSION OF RESULTS

Effect of Carbon Dioxide.—In the present study the solutions were not protected from exposure to air as it was intended that the results should be applicable to pharmaceutical dispensing under practical conditions. Brown and Cranston (8) obtained *p*H values of 5.67, 5.57 and 5.58 for *M*/10, *M*/100 and *M*/1000 solutions of zinc sulfate, respectively. In absence of carbon dioxide the corresponding *p*H values were 5.69, 6.27 and 6.77, respectively. The difference in *p*H in absence of carbon dioxide apparently is greater in the more dilute solutions of zinc salts.

Variation of *p*H with Time.—The results in Table III show that in general the *p*H of solutions of zinc salts remains unchanged or increases slightly after standing for a few days. Any rise is probably due to a combination of factors including leaching of alkali from the glass, removal of carbon dioxide from solution by chemical or physical combination with the precipitates or colloids formed, and changes in carbon dioxide equilibrium with varying temperature.

Hydrolysis of Zinc Salts.—Calculations of percentage hydrolysis may be made from *p*H data. In the case of zinc salts, the results of such calculations must be regarded merely as rough approximations for the following reasons: (*a*) the usual formulas do not strictly hold because zinc salts are salts of an insoluble base, (*b*) the salts of a bivalent metal may hydrolyze in two different ways, i.e., to basic salt or hydroxide, (*c*) the colloidal basic salts or hydroxide of zinc may adsorb or combine with hydrogen ions, (*d*) no definite equilibria are attained. Having these sources of error made in mind, calculations were made in the usual way (9) and it was found that the degree of hydrolysis in the solutions used in the present investigation was of the order of a few hundredths of a per cent, ranging up to about 0.1%.

The conclusion that zinc salts hydrolyze to only a very slight extent is confirmed by the results in Table III. Pure redistilled water in equilibrium with carbon dioxide of the atmosphere has a *p*H of 5.7. Table III shows that all of the *M*/1000 solutions studied, as well as some of the *M*/100 and *M*/10 solutions, had a *p*H higher than 5.7. The zinc salt thus reduced the acidity of the distilled water, probably by removal of some of the carbon dioxide by chemical or physical combination with the zinc compounds.

TABLE III.—AVERAGE *p*H VALUES OF SOLUTIONS OF ZINC SALTS BEFORE AND AFTER STORAGE

Concentration	Age of Solution in Days 0	2	4
	Zinc Acetate		
M/1000	6.5	6.5	6.5
M/100	6.7	6.6	6.6
M/10	6.5	6.5	6.5
	Zinc Bromide		
M/1000	6.4	6.2	6.3
M/100	6.3	6.3	6.3
M/10	6.2	6.2	6.2
	Zinc Chloride		
M/1000	6.1	6.4	6.5
M/100	6.5	6.5	6.3
M/10	6.1	6.2	6.2
	Zinc Iodide		
M/1000	5.9	6.1	6.4
M/100	5.9	6.0	5.9
M/10	5.5	5.5	5.5
	Zinc Nitrate		
M/1000	6.9	6.9	6.9
M/100	5.6	6.0	6.3
M/10	5.6	5.8	5.5
	Zinc Sulfate		
M/1000	6.0	6.2	6.2
M/100	5.7	5.7	5.8
M/10	5.2	5.2	5.2

SUMMARY

Determinations were made of the *p*H values of solutions of a number of zinc salts, using the glass electrode. A study was made of the changes in *p*H caused by heating, storage and recrystallization of the zinc salts.

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Effect of Time and Temperature in the Preparation of Certain Fats and Waxes for Melting-Point Determinations*,†

By D. M. Copley‡

As a result of certain discrepancies appearing in an earlier investigation of cocoa butter standards (1), a study of the official time and temperature conditions specified in the preparation of melting-point samples of Class II (2) fats and waxes was undertaken. These conditions are either contact of the charged melting-point tube with ice for at least two hours, or exposure to a temperature of 10° C., or lower, for twenty-four hours (3).

The study was designed to determine whether the molten fats and waxes, drawn into U. S. P. melting-point tubes, will return to normal solidification having constant melting points under the preparatory conditions of time and temperature now official. At the same time the possibility of congealing points as alternate or supporting standards was made a part of the investigation.

The official Class II fats and waxes requiring melting-point determinations are lard, wool fat, beeswax, spermaceti, cocoa butter and mutton suet. Samples of these were distributed for cooperative determinations, and since cocoa butter is produced by pressing and by solvent extraction methods, both types were included. Consequently all determinations were made on identical samples of each of the various fats and waxes.

EXPERIMENTAL

The following procedures were applied. After receipt, the samples were allowed to stand at least three days at room temperature before using. Melting-point tubes were charged with the molten fats and waxes, as specified in the U. S. P. XII (3) and additional tubes prepared by boring into the unmelted material. These latter samples were used for melting-point determinations without further treatment.

The remaining tubes, originally charged with molten materials, were subdivided into groups, and treated variously as follows: contact with ice for two hours, refrigeration at 10° C. or lower for twenty-four hours, for forty-eight hours and for seventy-two hours. Additional cocoa butter samples were prepared by charging melting-point tubes with the molten fat, chilling at 10° C. or below for thirty minutes, then allowing to stand at room temperature for twenty-four hours, forty-eight hours and seventy-two hours, respectively. Upon the expiration of the time periods specified above, melting points were determined by the U. S. P. XII method for Class II materials (3). Also, congealing points were determined by the official method (4) and in one instance cooling times and temperatures were plotted in the form of graphs as a possibility toward greater accuracy.

The findings of the various laboratories were accumulated in tabular form for ready reference and examination, appearing in Tables I to IX.

DISCUSSION

It is apparent that the over-all deviations in melting-point findings were rather wide, particularly in the cases of lard and wool fat. Beeswax, spermaceti and mutton suet were better, but lack the concordance expected of such quantitative procedures. Cocoa butter behaved abnormally throughout, always showing melting points below those of the original previously unmelted samples. These discrepancies, with the possible exception of the cocoa butter findings, indicate frequent substantial differences of opinion, even among experienced operators and upon identical samples, as to the true point of rise, or melting point.

Consequently, valid conclusions as to the effect of preparatory time and temperature cannot be based upon comparison between the various laboratories, but rather upon concordance within each laboratory in relation to the series of preparatory conditions. On this basis, and accepting personal judgment within each laboratory as reasonably constant, the official procedure for the preparation of these melting-point samples seems satisfactory in the cases of lard, wool fat, beeswax, spermaceti and mutton suet.

In general, charging the melting-point tubes with the fat or wax at room temperature is not a good procedure. The starting temperature and consistency may vary over quite a range, and in the case of the harder materials, particularly spermaceti, there are varying degrees of contact between the wax and the tube, affecting the point at which the melt rises.

Cocoa butter, both pressed and solvent extracted, is the serious exception. Under current preparatory requirements, the melting points are sharply depressed, often falling well outside of the permissive tolerance, even when the period of chilling is extended to seventy-two hours. Substantial improvement appears in the series wherein an initial thirty-minute chilling is followed by varying periods at room temperature. It is possible that refinement of these conditions, particularly a definition of the term "room temperature," may result in much more satisfactory conditions. Since a wait of twenty-four

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‡ Chairman of the Cooperating Subcommittee which is composed of the following members: F. J. Austin, William R. Warner and Co.; R. A. Cain, Sharp and Dohme, Inc.; S. H. Fox and C. L. Stump, Gelatin Products Co.; E. C. Merrill, United Drug Co.; W. J. Rice, Eli Lilly and Co.; Joseph Rosin, Merck and Co., Inc.; E. B. Vliet, Abbott Laboratories; L. A. Watt and F. D. Smith, Monsanto Chemical Co.

TABLE I.—MATERIAL: LARD

	Laboratory								
	A	B	C	D	E	F	G	H	I
Tubes filled cold	41.0	28.0		32.8	33.5	30.8	28.5	26.0	39.0
	41.0	29.0	31.5	32.4	34.0	30.8	27.8	30.1	39.0
	[a]	28.0			36.4				
		29.0			34.6 [b]				
On ice 2 hr.	37.5	39.0		29.6	33.0	37.3	30.5	33.0	38.5
	38.5	39.0	30.5	29.4	37.3	37.3	29.8	34.5	38.5
Chilled 24 hr.	38.0	37.5		30.8	32.0	37.2	29.5	29.4	39.0
	38.0	39.5	29.5	30.9	33.5	37.4	32.5	31.5	39.0
Chilled 48 hr.	37.5	37.5		28.5	30.3	38.2	30.0	35.5	37.5
	37.5	38.0	29.0	28.6	31.5	38.2	31.3	36.1	38.0
					32.5				
					32.3				
Chilled 72 hr.	39.0	37.5		28.4	32.0	37.9	33.5	35.5	36.5
	41.0	39.5	29.0	28.5	30.0	37.9	34.0	35.8	36.0
					31.0				
					33.6				
Congealing point	23.0	26.0		22.2		27.4	25.2	25.9	25.5
	20.0 [e]	26.0	30.2	[c]	31.8 [f]	[d]	25.0	25.9	24.5

[a] Creeps up tube slowly. Read when rate of rise increased.
[b] Behaves contrary to general behavior of most other fats.
[c] From curve 25.0. Considers U. S. P. method to allow too much latitude in judgment.
[d] First crystal.
[e] Indefinite.
[f] Not considered satisfactory. Special method used.

TABLE II.—MATERIAL: WOOL FAT

	Laboratory								
	A	B	C	D	E	F	G	H	I
Tubes filled cold	37.5	37.5		37.3	37.8	32.0	37.0	34.4	36.5
	38.0	33.0	42.0	37.3		33.0	39.0	34.6	37.5
	[a]	38.5						[b]	
		33.0							
On ice 2 hr.	38.0	47.0		38.1		38.1	37.0	37.6	39.0
	38.0	47.0	42.2	37.8	38.8	39.1	36.6	38.0	39.5
	[a]							[b]	
Chilled 24 hr.	38.5	48.0		35.9		35.5	39.0	37.5	39.0
	39.0	48.0	41.8	35.9	38.5	35.8	39.3	38.1	39.5
	[a]							[b]	
Chilled 48 hr.	39.5	47.5		36.9		36.4	39.6	38.1	41.0
	39.8	47.5	40.8	37.3	38.9	36.6	39.6	38.1	41.0
	[a]							[b]	
Chilled 72 hr.	38.8	48.5		37.6		36.3	38.8	38.1	40.0
	39.0	48.5	40.3	37.7	39.5	36.4	37.3	38.1	41.0
	[a]							[b]	
Congealing point	31.0	35.0		33.5		37.0	36.0	32.3	35.0
	32.0 [d]	34.0	39.0	[c]	38.5		35.2	33.0	35.5

[a] Creeps up tube slowly. Read when rate of rise increased.
[b] Rises slowly in tube. Figures only approximate.
[c] From curve 32.3.
[d] Indefinite.

TABLE III.—MATERIAL: BEESWAX

	Laboratory								
	A	B	C	D	E	F	G	H	I
Tubes filled cold	62.0	63.5	63.9	61.6	62.8	64.8	61.2	62.5	64.5
	62.0	63.5		61.3		65.9	62.5	62.7	64.5
On ice 2 hr.	63.8	67.0	65.4	64.5	64.2	64.0	64.3	64.2	64.5
	64.0	67.0		64.5		64.5	63.8	64.4	65.0
Chilled 24 hr.	64.0	66.0	65.4	64.3	63.8	64.5	64.3	64.7	64.5
	64.3	66.0		64.4		64.3	64.5	64.9	65.0
Chilled 48 hr.	64.3	66.0	65.5	63.7	63.8	64.7	63.6	64.5	64.5
	64.5	66.0		63.7		65.0	64.6	64.5	65.0
Chilled 72 hr.	63.0	65.5	65.8	64.1	64.0	64.2	63.8	64.4	64.5
	64.0	66.5		64.3		64.5	64.3	64.4	64.5
Congealing point	62.5	64.0	63.0	62.0	63.2	63.5	63.0	63.2	63.0
	63.0	63.0		[a]		[b]	62.5	63.3	63.0

[a] From curve 63.0. [b] Rise point.

TABLE IV.—MATERIAL: SPERMACETI

	Laboratory								
	A	B	C	D	E	F	G	H	I
Tubes filled cold	41.5	45.0		44.2		46.2	45.2	45.2	45.5
	44.0	46.0	44.2	44.5	45.0	46.5	45.4	45.4	46.0
On ice 2 hr.	[a] 46.5	46.0		44.8		45.5	45.7	45.7	46.0
	46.5	46.0	45.8	44.8	45.2	45.5	45.7	45.7	46.0
Chilled 24 hr.	46.3	45.5	46.2	43.9	45.3	45.2	45.6	45.6	46.0
	46.3	46.0		44.1		45.2	45.6	45.6	46.0
Chilled 48 hr.	46.3	45.5	46.2	45.2	45.4	45.2	45.7	45.7	46.0
	46.5	45.5		45.1		45.7	45.7	45.7	46.0
Chilled 72 hr.	46.3	44.0	46.3	44.2	45.3	45.7	45.8	45.8	46.5
	46.8	46.0		44.6		45.8	45.8	45.8	46.0
Congealing point	46.0	45.5	45.5	45.5	45.3	45.7	45.1	45.1	46.0
	46.0	45.5		[b]		[c]	45.1	45.1	45.5

[a] Point of rise depends on how it clings to the tube.
[b] From curve 45.7.
[c] Hold point.

TABLE V.—MATERIAL: COCOA BUTTER, PRESSED

	Laboratory								
	A	B	C	D	E	F	G	H	I
Tubes filled cold	35.0	37.5	36.5	34.0	33.7	34.9	35.2	35.6	36.5
	35.0	37.0		33.9	[a]	34.9	34.8	35.6	36.5
On ice 2 hr.	28.0	27.5	22.5	[b]	Below	28.1	30.8	Below	27.0
	28.0	27.5			24.0	28.2	31.8	25.0	27.5
Chilled 24 hr.	28.5	27.0	31.6	[b]	28.3	27.6	32.2		27.5
	28.5	27.5				27.3	32.2		28.0
Chilled 48 hr.	29.0	27.0	31.3	[b]	27.9	27.6	32.2		28.5
	29.0	27.0				27.6	32.2		29.0
Chilled 72 hr.	28.0	27.5	30.9	[b]	31.9	27.3	32.3		29.0
	28.0	27.5				27.5	32.0		29.0
Congealing point	26.5	22.0	18.3	25.0	33.0	21.2	27.0	26.5	18.0
	27.0	23.0	[c]	[d]	33.0 [f]	[e]	27.5	26.5	18.5

[a] Behaves contrary to general behavior of most other fats.
[b] Became liquid on returning to room temperature.
[c] Indefinite.
[d] From curve 25.7.
[e] First crystal.
[f] Not considered satisfactory; special method used.

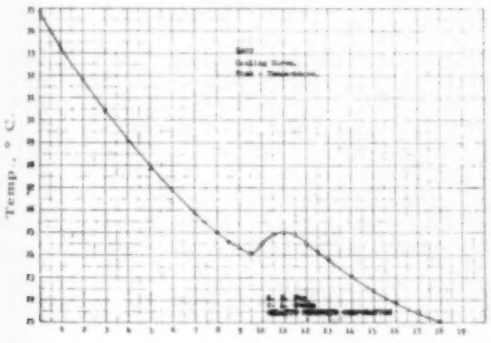

Fig. 1.

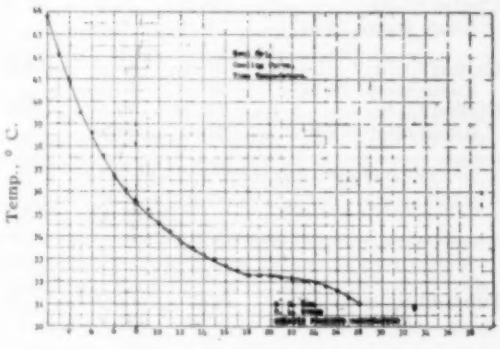

Fig. 2.

to seventy-two hours for the conditioning of the samples is a nuisance in a busy control laboratory, more rapid treatment would be advantageous. Preparatory super-chilling has been suggested. The study upon cocoa butter is to be continued.

Congealing-point concordance was largely disappointing. The results upon lard, wool fat and cocoa butter showed wide over-all divergence and were generally erratic. The results upon beeswax and spermaceti were much better, but these also responded better to melting-point determinations. Mutton suet now has an official congealing temperature requirement. This investigation showed a fair agreement between laboratories in these determinations upon mutton suet, an occasional marked deviation appearing in an otherwise generally uniform series.

One cooperating laboratory attempted to nullify

TABLE VI.—MATERIAL: COCOA BUTTER, SOLVENT EXTRACTED

	Laboratory								
	A	B	C	D	E	F	G	H	I
Tubes filled cold	35.0	36.5	36.2	33.4	33.6	33.1	35.4	35.1	36.5
	35.0	36.5		33.5	[a]	34.0	35.2	35.2	36.5
On ice 2 hr.	28.5	27.0	25.5	[b]	Below	27.4	31.5	Below	26.5
	28.5	27.5			24.0	27.4	30.2	25.0	25.5
Chilled 24 hr.	32.5	27.0	31.7	[b]	27.8	27.4	30.8		27.0
	33.0	27.0				27.4	31.0		27.0
Chilled 48 hr.	32.0	27.0	31.3	[b]	27.8	27.4	31.8		27.0
	32.3	26.5			[c]	27.4	31.8		27.0
					31.7 [d]				
Chilled 72 hr.	29.0	27.5	30.8		30.3	27.0	32.2		27.5
	29.0	28.0			30.8	27.2	31.8		27.5
					31.6				
Congealing point	27.0	23.0	17.2	26.2	32.8	20.3	26.8	26.0	17.0
	27.0	23.0	[e]	[f]	32.8 [h]	[g]	26.5	26.0	17.5

[a] Behaves contrary to general behavior of most other fats.
[b] Became liquid upon returning to room temperature.
[c] Partial.
[d] Complete.
[e] Indefinite.
[f] From curve 24.5.
[g] First crystal.
[h] Not considered satisfactory; special method used.

TABLE VII.—MATERIAL: COCOA BUTTER, PRESSED

	Laboratory								
	A	B	C	D	E	F	G	H	I
Chilled 1/2 hr.	35.0	36.0	33.5	32.9	33.6	33.2	32.0	35.6	32.5
Room temp. 24 hr.	35.0	36.0		32.9		33.2	31.5	35.8	32.5
	[a]								
Chilled 1/2 hr.	34.0	36.5	33.3	33.7	33.8	33.7	32.5	36.1	34.0
Room temp. 48 hr.	34.3	37.0		33.6		34.0	32.5	36.1	34.5
Chilled 1/2 hr.	34.0	37.0	33.8	33.7	34.0	34.2	32.5	36.1	34.0
Room temp. 72 hr.	34.0	37.5		33.9		34.4	32.8	35.9	34.0

[a] Film of oil rose at 33.5.

TABLE VIII.—MATERIAL: COCOA BUTTER, SOLVENT EXTRACTED

	Laboratory								
	A	B	C	D	E	F	G	H	I
Chilled 1/2 hr.	35.0	35.0	33.5	33.1	33.6	32.9	31.0	35.1	29.5
Room temp. 24 hr.	34.0	35.5		33.0		32.9	31.8	34.8	30.0
	[a]								
Chilled 1/2 hr.	34.0	35.5	33.5	33.5	33.3	33.3	31.5	35.1	33.5
Room temp. 48 hr.	34.0	36.0		33.5		33.7	32.3	35.1	34.0
Chilled 1/2 hr.	34.0	36.0	33.9	34.1	34.0	33.4	32.5	34.7	32.5
Room temp. 72 hr.	34.0	36.5		34.2		33.6	32.5	34.7	33.0

[a] Column separated, rose in two parts, at 34.0 and 35.0.

TABLE IX.—MATERIAL: MUTTON SUET

	Laboratory								
	A	B	C	D	E	F	G	H	I
Tubes filled cold	51.8	52.0	51.0	50.5	50.8	51.0	50.6	51.4	52.5
	52.0	52.0		50.4		51.0	49.9	51.5	53.0
	[a]								
On ice 2 hr.	50.5	51.5	51.2	50.3	50.8	50.7	51.4	51.4	52.0
	51.0	51.5		50.4		51.0	51.2	51.5	52.5
Chilled 24 hr.	51.0	53.0	51.1	50.4	50.1	50.8	51.4	51.5	52.0
	51.0	53.0		50.5		50.9	51.1	51.5	52.5
		53.0							
		52.5							
Chilled 48 hr.	50.5	52.0	51.0	50.2	50.4	51.0	51.1	51.5	51.5
	51.0	52.0		50.1		51.3	51.4	51.5	51.5
Chilled 72 hr.	50.5	51.5	50.3	50.4	50.3	50.4	50.9	51.4	52.0
	50.8	52.0		50.3		50.8	50.4	51.5	51.5
Congealing point	40.0	41.0		40.5		44.2	36.3	47.0	39.5
	40.0	40.0	40.0	[b]	39.5		36.8	47.9	38.5

[a] Column split in sections. Reading last section to rise.
[b] From curve 43.5.

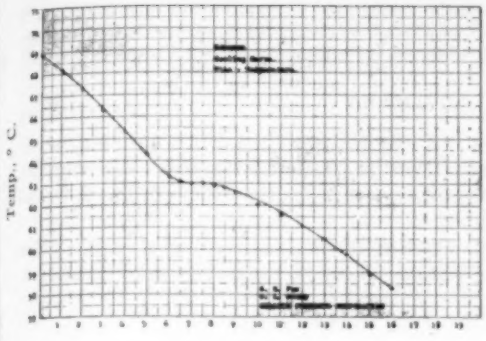

Fig. 3.

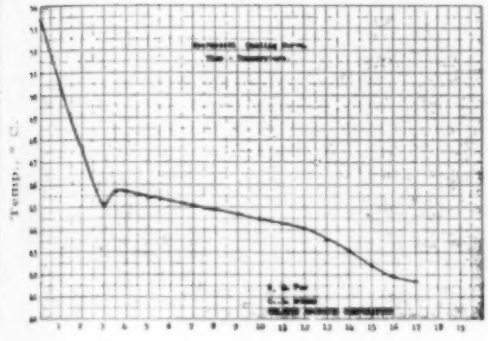

Fig. 4.

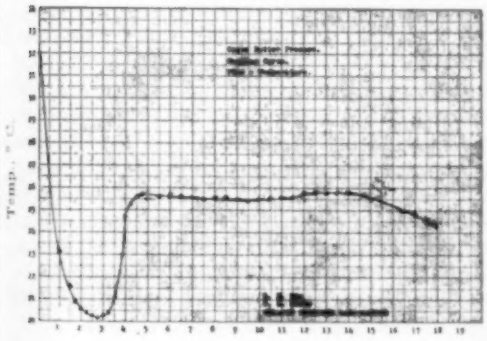

Fig. 5.

the factor of personal judgment by plotting the time and temperature during the cooling of the test samples, the results appearing in Figs. 1 to 7. This method of recording has interesting possibilities. It leaves little doubt as to "the highest temperature remaining constant for a short time" and in addition illustrates the varying behavior of the different fats and waxes under this test. While this method was not included in the original plan of investigation and consequently is unsupported by cooperative trials, it is included in this report as a possible stimulus to more exacting study of this point.

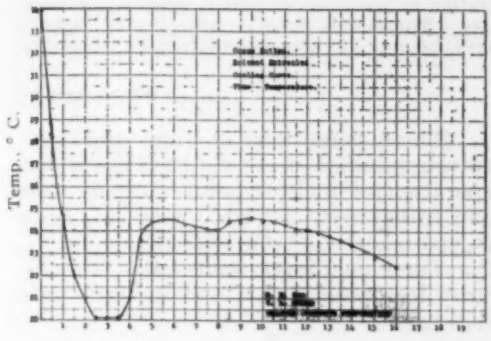

Fig. 6.

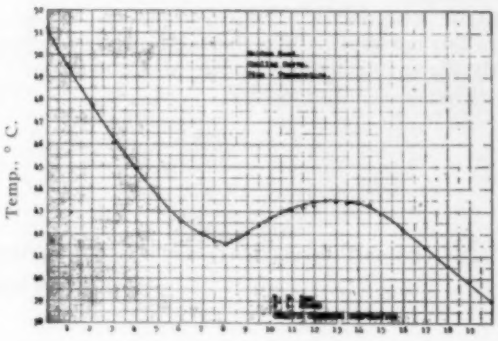

Fig. 7.

Comment.—Although this project was not designed to include factors beyond the preparatory time and temperature conditions for Class II melting-point determinations, the numerous instances of apparently undue variation in results caused consideration to be given to the latter steps of the method.

There seems to be considerable confusion as to the meaning of the term "melting point." In the case of fats containing a mixture of components there may be several degrees' difference between the beginning of melting and the final point of complete fluidity and transparency.

There have been many methods devised for determining such melting points, indicating by their very multiplicity the uncertainty which surrounds this property. In any method such as that of the U. S. P. XII, where any external influence other than temperature affects the results, the reading is taken at a point which indicates a certain marked degree of softening or, at the most, a liquefaction of the lower melting fractions. On the other hand, any method which calls for a total melt as the end point is defining melting point as the upper end of the range. It would seem that a definition of just what property is being measured could lead to substantial improvement. One authority in this field (5) recognizes three descriptive terms, melting point, softening point and slipping point.

In a sense U. S. P. XII does define the property and the conditions, but under these conditions the melting point is more truly a softening point and the capillary tube method is subject to varying inter-

pretation in numerous instances, as shown in these tables. The standard for a softening or slipping point is bound to be somewhat arbitrary, depending upon the method of determination specified, but a method even though giving arbitrary but more constant results between laboratories would be helpful.

CONCLUSIONS AND SUMMARY

1. These conditions of time and temperature specified in U. S. P. XII for the preparation of melting-point samples were found satisfactory for lard, wool fat, beeswax, spermaceti and mutton suet.

2. These conditions were found unsatisfactory for cocoa butter, and further study is indicated.

3. In general, charging the melting-point tubes with fats and waxes at room temperature was not a good procedure.

4. Congealing temperatures were not generally as satisfactory as melting points as control standards. There was a close parallel between these two characteristics with regard to concordance of determinations between laboratories.

5. A suggestion that time and temperature curves be plotted for greater accuracy in congealing temperature determination is included.

6. Some uncertainties related to the melting of Class II materials are discussed.

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(3) *Ibid.*, p. 596.

(4) *Ibid.*, p. 566.

(5) "Official Methods, American Oil Chemists Society," American Oil Chemists Society 1944, p. 33.

Notes on Mexican Drugs, Plants, and Foods. III. Ahuauhtli, the Mexican Caviar

*By Marcel Bachstez and Altagracia Aragon**

Prior to the conquest of Mexico, the natives were limited to a rather narrow selection of foods. Animal foods were especially limited since neither cattle, goats, nor sheep were known to them. Horses were unknown until Cortes invaded the continent. Life was maintained essentially by vegetables, corn, fish, and poultry, all of which seem to have been abundant.

Insects furnished a limited amount of food among which were certain items considered as delicacies. Among these was the "Ahuauhtli of Texcoco," which consists of the eggs of the "Axayácatl" (a fly-like insect), *Krizousacorixa azteca* Jacz, *Krizousacorixa texcocana* Jacz, and *Corisella mercenaria* Say. The name of the eggs is derived from the *Nahuatl* tongue, Atlhuautli, Atl = water and huautli = seed (1).

Until the outbreak of the present war, the dead flies, known as "Axayácatl," were exported in carload quantities to Holland and from there to Germany, supposedly for use in canary bird food. A Dutch company in existence in Mexico City until about 1938 purchased these flies from the natives of Texcoco, who brought them to the city in bags, obtaining as much as one peso twenty-five per kilo, then equivalent to about sixteen U. S. cents per pound.

At the beginning of the rainy season, the flies deposit their eggs in large quantities on the surface of the stagnant alkaline waters of Texcoco Lake and on the reeds growing in the lake. These eggs are collected by the natives during the entire season lasting from June until October, and are brought to the market to be sold. The eggs are white, about 0.5 to 1.0 mm. in diameter (Figs. 1 and 2) and are generally contaminated with particles of the reeds which adhere to them.

The Ahuauhtli have been used as a food for many centuries, their use probably originating long before the conquest of Hernan Cortes. The various foodstuffs used by the natives are described by Sahagun (2) (1499–1590), the most famous historian and possibly the only one who understood the Nahuatl and other native languages in his remarkable codex, "Historia de las cosas de la Nueva España" (1557). He states that at the court of the Emperor Moctezuma as well as of those Aztec kings that preceded him prior to the tenth century, the "Ahuauhtli" were especially prepared during

* Química Coyoacan, S. A., Coyoacan, D. F. Mexico.

the ceremony dedicated to the god Xiuhtecutli. They were considered a delicacy and were brought into Tenochtitlan by fast native runners from Texcoco so that the emperor would have them fresh for breakfast. Sahagun calls them "Aoauhtli" or "Ahuauhtli" and states that the common name used by the people was "aguaucle" which meant "seeds of the water." He states further that they were eggs deposited by flies on the surface of stagnant waters in infinite numbers, and were still being sold in the market place of Texcoco and other neighboring villages.

Fig. 1.—Ahuauhtli (Enlargement about 1 ×).

Most of the subsequent historians obtained their information from Sahagun, adding thereto their own observations gathered from native folklore. Thus Dr. Francisco Hernandez (3) (1649) and Francisco Clavijero (4) (1780), refer to them as food stating that the conquerors called them "the Mexican caviar," and Prescott (5), repeating Bernal Diaz del Castillo (6), the notable eyewitness of the conquest, states that they were usually eaten prepared with fowl eggs in the form of an omelette, remarking, however, that the "conquistadores" did not like them too well. Leon Coindet (7) (1867), speaking from the medical viewpoint, mentions the savoriness of these insect eggs. Today they may still be found on sale in the markets of the old town of Texcoco as well as at Los Reyes, a village bordering upon the lake, and at the La Merced and San Juan markets in Mexico City. Many of the typical Mexican restaurants serve them as a delicacy in much the same manner as they serve Magyue castus worms. The flavor is quite similar to that of crab or caviar.

We have been able to find but one paper in the scientific literature by Ancona (8), who gives a detailed account of the insect "Axayácatl" that lays the "Ahuauhtli," but were unable to find anything concerning the chemical composition of the eggs. It was therefore thought to be of considerable interest to investigate them chemically.

EXPERIMENTAL

The eggs were cleaned for analysis by removing the vegetable matter adhering to them. All determinations were run on the air-dried material, and the methods specified in the A. O. A. C. Methods of Analysis (9) were generally used. The ash obtained upon incineration of the eggs was analyzed for calcium, iron, potash, and sodium. The calcium was determined as oxalate and the iron was determined colorimetrically according to the method described by Elvehjem (10). The fat contains cholesterol as indicated by positive Salkowski (11) and Liebermann–Burchard reactions.

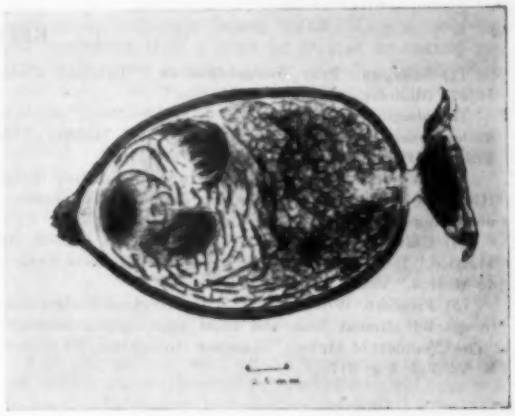

Fig. 2.—One Ahuauhtli Egg (Stained with Carmine). Scale—0.1 Mm.

The eggs were digested with potassium hydroxide solution, which mixture upon distillation produced volatile bases possessing a caviar-like odor. The distillate was titrated and the N-value subtracted from the protein determination according to Kjeldahl. A phospholipid was isolated by extraction, which is soluble in ordinary solvents but is precipitated by acetone, and is probably lecithin. The lecithin was also calculated from the phosphorous content. Results are given in Table I.

TABLE I

Moisture (at 100° C.)	9.3%
Ash	6.3%
Calcium	0.33%
Iron	0.20%
Fat	5.7%
Protein	77.0%
Lecithin	17.4%
Phosphorus	0.73%

For the characterization of the protein, 3 Gm. of the eggs was hydrolyzed with hydrochloric acid (12). The content of acid-insoluble nitrogen was 0.4%. The hydrolytic solution was repeatedly evaporated with water under a vacuum and finally brought to dryness. The residue gave the following reactions (13):

Biuret: weakly positive (histidine and peptones)
Millon: negative (no tyrosine)
Knoop: positive (histidine)
Pauly: positive (histidine)
H_2S: weakly positive (cystine)
Rosenheim, Adamkiewicz: negative (no tryptophane)
Sakaguchi: positive (arginine).

The fractional portions obtained by the hydrolysis are therefore principally histidine and arginine.

SUMMARY AND CONCLUSIONS

1. The "Ahuauhtli" eggs of the insect "Axayácatl" have been studied and their chemical composition determined by the experiments herein reported.

2. The results show: water 9.3%; ash 6.5%, with calcium 0.33%, iron 0.20%; fat 5.7%; protein 77.0% and lecithin 17.4%.

3. Upon hydrolysis the protein gave principally histidine and arginine.

4. The "Ahuauhtli" have a food value because of their high protein content.

5. They may be an economical source of histidine and arginine and it is recommended that the commercial possibility be further investigated.

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(12) Morrow, C. A., "Biochemical Laboratory Methods," John Wiley and Sons, New York, 1935, p. 130.

(13) *Ibid.*, p. 107.

The Subacute Toxicity and Irritation of Polyethylene Glycols of Approximate Molecular Weights of 200, 300, and 400*

By Henry F. Smyth, Jr., Charles P. Carpenter, and C. Boyd Shaffer†

Polyethylene glycols are being considered as solvents, hygroscopic agents, vehicles, and thickening agents in a number of preparations intended for application upon the human dermis, and are being introduced prudently into commerce. It is recognized that ethylene and diethylene glycols manifest a high degree of cumulative action upon the kidney when they reach the circulation (1). Some of us (2) have shown that polyethylene glycols of high molecular weight do not share this objectionable property. In the series between these extremes there are available several products about whose toxicity nothing has yet been published.

Polyethylene glycols 200, 300, and 400 are commercially available mixtures, each representing compounds within a band of molecular weights, the average of which is used in characterizing the compound. They are viscous light-colored fluids with high boiling points, and are completely soluble in water. They also dissolve in aliphatic ketones, alcohols, and esters, in glycol ethers and aromatic hydrocarbons.

* Received Dec. 7, 1944, from the Mellon Institute for Industrial Research, Pittsburgh, Pa.

† With the assistance of other members of the Multiple Industrial Fellowship on Chemical Hygiene.

EXPERIMENTAL

Single Dose Oral Toxicity.—Single doses of the undiluted materials were administered by stomach tube to male albino Wistar strain rats weighing 90 to 120 Gm. Male albino rabbits, of approximately 2.5 Kg. weight, similarly received doses of 50% aqueous solutions. Survivors were observed for fourteen days. Median lethal doses (LD_{50}'s) were calculated by the method of Bliss (3) and are listed below together with the usual fiducial limits ($\pm 1.96 \times$ the standard deviation), in terms of Gm. of polyglycol per Kg. body weight.

	Rats	Rabbits
Polyethylene glycol 200	28.9 (25.7-32.5)	19.9 (17.0-23.4)
Polyethylene glycol 300	31.7 (28.4-35.5)	20.7 (18.9-22.7)
Polyethylene glycol 400	32.8 (28.8-37.4)	26.8 (24.3-29.6)

The LD_{50} values for rats are not significantly different, but that for rabbits receiving PEG 400 is significantly greater than for the other two glycols.

The majority of the animals receiving doses of the glycols either died within twenty-four hours or survived and gained weight normally during the fourteen-day observation period. The only gross pathology observed in those killed by the glycols was congestion of the digestive tract.

Subacute Oral Toxicity.—Each of the three polyglycols was administered to 5 male albino rats in drinking water in concentrations of 16, 4, 1, 0.25, and 0.06 Gm. per 100 ml., with 10 rats receiving pure water to serve as control animals. These solutions were the sole source of water for ninety days. The average dosages in Gm. per Kg. per day were calculated following daily measurement of the volume drunk by each group of 5 rats.

The animals were weighed each week. After about eighty days on the regimen blood counts were performed on those drinking 4% solutions, the urine of all groups was subjected to routine analytical procedures, oxalic acid in the urine was sought particularly, and the concentration of urea nitrogen in the blood was estimated. Histopathological studies were performed upon adrenal, small intestine, kidney, liver, spleen, and testis.

No abnormalities in volume of fluid drunk, growth, behavior, blood count, blood and urine chemistry, or micropathology were found in any rat consuming 4% solutions as the sole source of water. The dosages of polyethylene glycols 200, 300, and 400 received by these rats were respectively 4.8, 5.4, and 4.8 Gm./Kg./day, or approximately one-sixth the LD_{50} per day for ninety days.

Rats receiving 16% solutions drank from one-fourth to three-fourths as much fluid as did the control rats and their growth was quite irregular but always significantly less than normal. Two-thirds of these rats died, those receiving polyethylene glycols 200 and 300 within nine days and those drinking polyethylene glycol 400 in eighty to eighty-four days. One, two, and two rats on the three fluids, respectively, survived the full ninety days. The organs of those surviving polyethylene glycols 200 and 400 were normal, but those surviving polyethylene glycol 300 revealed marked cloudy swelling of the livers and excessive dilation of kidney glomeruli, probably not due to low water intake. The rats dying after drinking this concentration of the polyglycols showed, in addition to these effects, nuclear degeneration of the convoluted kidney tubules. No oxalic acid was found in the urine and no crystals of calcium oxalate were present in the kidneys. The dosages they consumed were 10.9, 20.5, and 16.4 Gm./Kg./day of polyethylene glycols 200, 300, and 400, equivalent to one-third to two-thirds LD_{50} per day.

Single Skin Absorption.—The undiluted polyglycols were applied to the skins of 6 rabbits each using a modification of the cuff test of the Food and Drug Administration (4). The largest dosage practical to apply was 20 ml./Kg., in this case approximately the oral LD_{50} for the species. No rabbit died from this application of polyethylene glycol 300 or 400 and one of 6 from polyethylene glycol 200.

Subacute Toxicity by Skin Absorption.—The three polyglycols in dosages of 2 ml./Kg./day were each applied to the clipped abdomen of 6 albino rabbits five days a week for eighteen weeks. The doses were rubbed into the skin by gentle inunction before the animals were released. No animals died, none failed to gain weight regularly, and there developed no micropathology in adrenal, kidney, liver, spleen, or testis. The skin at the site of inunction remained normal throughout the experiment. Blood urea nitrogen and serum icterus remained normal.

Irritation.—The three polyglycols were applied to the clipped abdomens of 6 albino rabbits in the test this laboratory standardized for evaulating certain insect repellents. Rabbits were first selected which showed a maximum reaction to a particular chemical compound used as a reference standard. They were immobilized on their backs and marked areas on the abdomen were kept moist with the test material for four hours. None of the polyglycols produced any congestion or any other sign of irritation during the test or twenty-four hours later. Experience has demonstrated that a slightly greater irritation can be tolerated in a preparation intended for application to the human cutis. A further substantiation of their blandness upon the rabbit abdomen exists in the ninety-day inunction application already described. No irritation was found from the polyglycols.

In contact with the rabbit conjunctiva, averaging the results with at least 5 animals, a 20% solution of polyethylene glycol 200 in isotonic saline was slightly less irritating than a 10% solution of glycerin U. S. P. in saline, 20% polyethylene glycol 300 was slightly more irritating, and polyethylene glycol 400 was equally irritating as the glycerin. The differences were slight.

The polyglycols were added undiluted to the rabbit eye for the purpose of producing corneal necrosis, to be detected eighteen, to twenty-four hours later by fluorescein staining; the usual practice in this laboratory with all new products tested. The reactions were quantitatively similar to those with liquid petroleum U. S. P., in that each polyglycol caused a trace of diffuse necrosis in one or two eyes of five tested. No necrosis was produced by 15% aqueous solutions. Such diffuse necrosis heals rapidly, and would probably be detected in the human eye only as a brief smarting similar to that caused by soap.

The three polyglycols were applied in the patch test upon the backs of 23 male college students. They remained on the students' backs seven days, and after a ten-day period they were reapplied for two days. On this limited group of subjects polyethylene glycol 400 was equivalent to cocoa butter (4% of subjects gave definite erythema), polyethylene glycol 300 to lanolin (9% definite erythema), and polyethylene glycol 200 somewhat more irritating (22% definite erythema).

DISCUSSION

When the results related in the present communication are combined with those of our paper (2) upon similar compounds of higher molecular weight and an earlier contribution (5) upon glycol derivatives it is seen that there is a rather uniform decrease in single dose oral toxicity as the molecular weight is increased in the series of polyethylene glycols. Our last article (2) failed to mention that "Carbowax" compound 1500 is actually a mixture in approximately equal proportions of polyethylene glycol 300 and "Carbowax" compound 1540. Its oral LD_{50}

for rats (44.2 Gm./Kg.) is, as would be expected, midway between those of its components (31.7 and 51.3 Gm./Kg.).

When the toxicity of repeated oral doses is considered the series of glycols appears to be less uniform. Ethylene and diethylene glycols manifest a high degree of cumulative action. Polyethylene glycols with average molecular weights of 200 to 400 did not injure rats at a dosage level of approximately 5 Gm./Kg./day for 90 days. The similar safe rat dosage of "Carbowax" compound 1500 was 1.5 Gm./Kg./day, and of "Carbowax" compound 4000 was 0.04 Gm./Kg./day. The reasons for the cumulative action of the higher molecular weight compounds in the series are not now known, but work now in progress may elucidate the matter.

None of the compounds with average molecular weights of 200 or more injured rabbits through skin penetration over a ninety-day period and the irritating properties are negligible.

SUMMARY

Commercial products known as polyethylene glycols 200, 300, and 400 were found to have a low order of single dose oral toxicity to rats and rabbits. Their subacute toxicity studied over a ninety-day period in rats by mouth and rabbits by inunction was also of a low order. The irritation of these chemicals is not greater than that of materials commonly applied to the human skin.

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Cascara Sagrada Berries, an Adulterant of Buckthorn Berries, N. F. VII*

By Clare Olin Ewing† and Albin Stitt‡

Buckthorn berries, N. F., are one of the lesser members of the group of official laxatives and cathartics that owe their efficacy to anthraquinone compounds of glycosidal character. They are obtained from a shrub, *Rhamnus cathartica* L., indigenous to Northern Africa and Central Asia but widely distributed in Europe and locally in the Eastern United States. Before the war commercial supplies were imported largely from Hungary. With the stoppage of supplies from this source, it was logical to seek domestic supplies.

Whether by reason of inexperience in collecting or by intention, some spurious buckthorn berries have appeared on the market. We have been obliged to reject several shipments and to purchase samples that consisted largely of the dried ripe fruit of *Rhamnus Purshiana* de Candolle. Identification was confirmed by comparison with specimens in the herbarium of the Arnold Arboretum of Harvard University. Macroscopically they bear a strong resemblance to the official berries, although they are slightly larger. They can be distinguished readily by reason of having only two to three flattened seedlike nutlets, whereas the official berries

TABLE I.—PRINCIPAL DISTINGUISHING CHARACTERISTICS BETWEEN BUCKTHORN AND CASCARA BERRIES

	Rhamnus cathartica	*Rhamnus purshiana*
Diameter of dried fruit, mm.	4–8	6–10
Number of nutlets	3–4	2–3
Transverse diameter of nutlet, mm.	2–3	4–5
Color of nutlet	Dark brown	Light to medium brown
Shape of nutlet	Triangular, convex, compressed	Slightly flattened, convex, broadly oval
Hilum	Tiny, inconspicuous, dull	Large, conspicuous, glabrous, lighter colored

* Received Sept. 1, 1944, from the Dept. of Research and Control, United Drug Company, Boston, Mass.

† Chief Chemist and Associate Director, Dept. of Research and Control, United Drug Company.

‡ Chief Control Chemist, United Drug Company.

possess three or four smaller compressed ones. The characteristics listed in Table I which will enable one to distinguish readily between the two nutlets are illustrated in Fig. 1 through the courtesy of our colleague, Mr. E. F. Tilc.

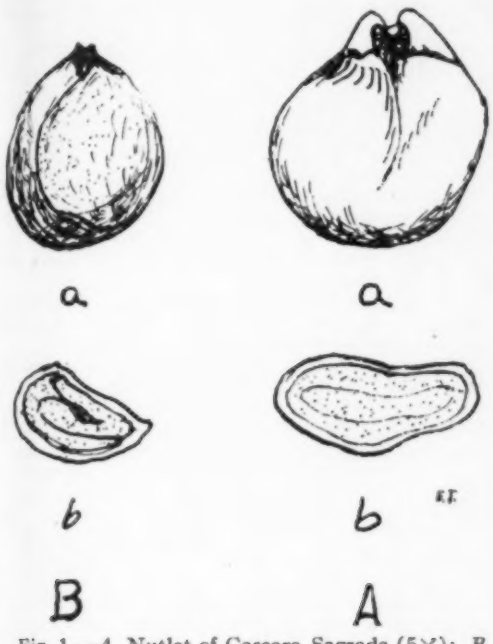

Fig. 1.—*A*. Nutlet of Cascara Sagrada (5×); *B*. Nutlet of Buckthorn Berries (5×). *a*. Macroscopic appearance; *b*. Transverse cross section.

Emodin Test.—Five grams of the spurious berries was boiled with 50 cc. of a 1 per cent KOH solution, cooled, filtered and acidified with dilute HCl. Ten cubic centimeters was extracted by shaking with 10 cc. of ether. The ether was decanted and shaken with 5 cc. of 10 per cent NH_4OH. The ammoniacal solution gave a reading of 1 Red on a Lovibond Tintometer. Authentic official buckthorn berries similarly treated gave a Lovibond reading of 12 Red. This shows that the spurious drug has less than one-tenth of the anthraquinone derivative content of the official buckthorn berries.

Although Zörnig (1) in 1909 included cascara berries in a list of adulterants of buckthorn berries, we have been unable to find them recorded in American texts or handbooks. Apparently they have not hitherto appeared on the American market as an adulterant of buckthorn berries. Inasmuch as *Rhamnus purshiana* is indigenous to the Washington-Oregon-British Columbia area of North America and is the basis for a thriving cascara bark industry, it is not surprising to find these berries appearing on the market. It is somewhat surprising that the berries showed so little active principle.

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(1) Zörnig, H., "Arzneidrogen," Werner Klinkhardt, Leipzig, 1909, p. 224.

Book Reviews

Organic Chemistry, with Applications to Pharmacy and Medicine, by ELDIN V. LYNN. Lea & Febiger, Philadelphia, 1945. 355 pp. Price, $4.50.

The author has planned a "texbook in organic chemistry that would also give the medical and pharmaceutical applications . . . that would review the basic reactions and apply them to the substances used in medicine and pharmacy."

Throughout the book a proper emphasis has been placed on nomenclature and isomerism. The material is presented in a logical manner and is properly organized. Among the subjects which are especially well presented is the chemistry of the olefines and aliphatic amines. Study of the subject matter, presented in forty-four chapters, is facilitated by carefully chosen questions at the end of each chapter. The thorough index should prove useful for reference to specific organic medicinal agents.

Various statements appear which might be confusing or are erroneous. The following were chosen as especially misleading: "Alkali bisulfites give crystalline compounds with alkyl methyl ketone but not with the alkyl alkyl variety" (p. 81). In reference to the reduction of aromatic nitro groups, the statement is made that "It is even possible to accomplish it with ordinary hydrogen at high temperature in the presence of metallic catalysts" (p. 195); although it is frequently necessary to dissipate the heat of the generally exothermic reaction. It is regrettable that the author did not choose the more practical method for the synthesis of sulfanilamide (p. 201) which involves the ammonolysis of *p*-acetaminobenzenesulfonyl chloride and subsequent hydrolysis of the acetyl group.

The text would be improved by the inclusion of more illustrative formulas and equations and by an elaboration in accordance with modern concepts of those sections dealing with the structure of benzene, valence, geometrical and optical isomerism.

It is the reviewer's opinion that the descriptions of medicinal products are comprehensive and commendable, but the inadequate space allotted to their chemistry will make the use of this book as a text of limited value in a first course in organic chemistry and the elementary treatment of medicinal products, unsatisfactory for more advanced students of organic chemistry.—GEORGE P. HAGER.

Fundamental Principles and Processes of Pharmacy, by HENRY M. BURLAGE, EDITOR, JOSEPH B. BURT, CHARLES O. LEE, and L. WAIT RISING. McGraw-Hill Book Company, New York, 1944. ix + 615 pp., illustrated. Price, $4.50.

The authors have written a clear, concise text on the material generally presented in beginning pharmacy courses. It is probably the best presentation of this subject matter that has yet been published.

The first six chapters which deal with the history, ethics, curriculum, opportunities, and literature of pharmacy, give an excellent over-all picture of the profession. No attempt is made to cover up the known weaknesses, but instead they are pointed out. This type of approach should be of great help and interest to beginning students. The section on "Pharmacy in the United States" is one of the high spots in these first chapters. The table on Development of Pharmacy in the United States, 1881–1915, is worthy of close scrutiny by both students and instructor.

Beginning with Chapter 7 and continuing through Chapter 19, the material covered is essentially the same as now presented in other introductory pharmacy texts. However, the information given is more complete and direct than in earlier references.

The chapter on metrology is to this reviewer's mind too detailed and lengthy. Much of the discussion of the systems of weights and measures could better be taken up in pharmaceutical calculations. The same is true of the material written on the analytical balance. It is admirably done, but should be given in Quantitative Analysis.

Some of the topics such as refraction, optical rotation, and measurement of surface tension are probably beyond the conception of the average freshman. Perhaps an exposure to these items will aid them in the more detailed study they will make of these subjects in other courses. The same statement to a lesser degree applies to the discussion of *p*H and isotonic factors given in later chapters.

There is some repetition when one author presents a slightly different phase of a subject covered earlier in the book by another author. This is not of sufficient importance to detract from the over-all excellence of the entire text.

Chapter 20, "The Natural Products Used in Pharmacy," is well done but seems out of place in this book. One of the features carried out up to this point is that no attempt is made (except briefly in the chapter on "Emulsions") to go into the pharmaceutical preparations and drugs which naturally belong in other courses. This last chapter deviates from that policy and could easily have been omitted.

In conclusion, one observation should be made: If a separate course is to be given in this material, the text will admirably fit that purpose. The question arises: Should this material be incorporated into other courses and not be taught separately?—TOM D. ROWE.

Outline of the Amino Acids and Proteins, edited by MELVILLE SAHYUN. Reinhold Publishing Company, New York, 1944. 251 pp. 14 x 23 cm. Price $4.00.

A number of comprehensive and detailed accounts of the chemistry of amino acids and proteins have been written during recent years. In addition, a number of reviews are available on an annual basis. However, all of these treatises suffer from too much detail for the student who has little or no background in this very complex field. The text that is reviewed here was written to fill in this void by providing a broad but somewhat elementary review of the entire field keeping the novice in mind.

In general this small outline fulfills its promise. It is the reviewer's opinion, however, that the unified viewpoint of a single author could better present such a vast subject on an elementary level. The "Outline of Amino Acids and Proteins" is a composite work written by thirteen authors under a single editorship. Each author is a recognized authority in his own field.

As would be expected from a book of this character, some of the chapters are superbly written while others leave considerable room for improvement. For example in the chapter on "Methods of Analysis" written by David M. Greenberg, the small section which deals with the solubility-product constant method of protein analysis developed by Bergman and co-workers, the description is so cursory that a casual reader would learn little from it. Yet in the same chapter, detailed methods are given for the determination of some of the individual amino acids.

In view of the immense interest in immunity reactions at present, Dr. Heidelberger's chapter on immunity reactions is disappointingly short.

The reviewer believes that the section on the role of the amino acids in detoxication by Professor Quick is quite inspiring because the viewpoint has been expanded over the more narrow concept of detoxication that is usually expressed in texts on biological chemistry. The sections on intermediate metabolism of proteins and amino acids by Dr. Cahill are exemplary for the author's treatment of controversial and complex issues.—MELVIN W. GREEN.

Advances in Protein Chemistry, edited by M. L. ANSON and JOHN T. EDSALL, Volume I. Academic Press, New York, 1944. xi + 341 pp. 14.5 x 23 cm. Price $5.50.

So many phases of modern research rest upon protein chemistry that the past few years have seen great strides made in the protein field. To keep up with such an active field, regular well-documented reviews are needed. This need has been met in part by a chapter in the "Annual Reviews of Biochemistry" and other occasional summaries. Now, fortunately, we are promised an annual "Advances in Protein Chemistry" which should serve effectively.

The first "Advances" contains the following reviews:

Lipoproteins, by Erwin Chargaff
Structural Proteins of Cells and Tissues, by Francis O. Schmitt
Some Contributions of Terminology to the Study of Proteins, by Henry P. Treffers
The Interaction between the Alkali Earth Cations, Particularly Calcium and Proteins, by David M. Greenberg
The Purification and Properties of Certain Protein Hormones, by Bacon F. Chow
Soybean Proteins in Human Nutrition, by Donald S. Payne and L. S. Stuart
Nucleoproteins, by Jesse P. Greenstein
The Proteins of Skeletal Muscle, by Kenneth Bailey

In general, the quality of the individual reviews is of the highest. Some evidence of the completeness of the literature coverage is gained from the fact that nearly one thousand different authors are represented in the bibliography. Careful editing has kept the overlapping of information at a minimum. The paper quality is very poor, unfortunately but is at present unavoidable.

It is to be hoped that this project will be continued.—MELVIN W. GREEN.